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# MEDICAL SCIENCE

## Abstracts & Reviews

### VOLUME IV

APRIL—SEPTEMBER 1921

Published for

THE MEDICAL RESEARCH COUNCIL

by

HUMPHREY MILFORD
OXFORD UNIVERSITY PRESS
LONDON EDINBURGH GLASGOW COPENHAGEN
NEW YORK TORONTO MELBOURNE CAPE TOWN
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# I. INDEX OF SUBJECTS

ABSTRACTS.
  Biochemistry, 84, 173, 273, 376, 468, 573.
  Neurology, 53, 146, 242, 347, 441, 547.
  Pathology and bacteriology, 57, 152, 255, 352, 450, 550.
  Radiology and electrology, 91, 181, 283, 388, 481, 581.
  Surgery, 52, 239, 341, 435.
Acacia-glucose solutions, influence of intravenous injections of, on urine secretion and blood-volume in rabbits, 277.
Acanthosis nigricans with carcinoma of internal organs, 114.
Acetaldehyde, identification of aldehyde-like substance in diabetic urine as, 576.
  as intermediary substance in fermentation of sugar by *B. lactis aerogenes*, 388.
  formation of, during decomposition of sugar by moulds, 388.
Aceto-nitrite reaction, 578.
Acidosis in toxaemias of pregnancy, 537.
Acriflavine, antiseptic potency of, 465.
Acromegaly, radiotherapy of, 582.
Actinomycetes, acid-fast, with report of case from which a new species was isolated, 261.
Actinotherapy of three cases of tumour of hypophysis, 486.
Addison's disease, cause of skin colour in, 231.
Adrenalin, effects of, on respiratory exchange, 274.
  glycaemia, 576.
  test for pancreatic insufficiency, 514.
  in treatment of erythromelalgia, 112.
Adrenals, post-operative depletion of epinephrin store of, 476.
Agglutinating sera, action of continuous electric current on, 355.
Agglutination, isoelectric point of red blood cells and its relation to, 176.
  and sedimentation of bacteria, 176.
Albuminous substances and saline solutions, 'intertraction' between, 577.
Alcohol, ethyl, influence of, on organism, 463.
Alimentary diseases, 3.
Alkali reserve of blood, relation of, to glycosuria and hyperglycaemia in pancreatic diabetes, 173.
Alopecia areata an abortive form of general syphilis, 113.
Amino-acids, oxidation of, by blood charcoal, 480.
'Ammonia coefficient' of pregnancy, 89.
Amoeba, parasitic, new species of, occurring in crypts of tonsils (*Entamoeba macrohyalina*), 457.
Amoebic abscess of liver, treatment of, 403.
Anaemia, acute experimental, blood phosphates in lipaemia produced by, 174.
  acute, lipaemia in, 88.
  severe, carbon dioxide absorption curve and carbon dioxide tension in, 381.
  splenic, 119.
Anaerobic flora of intestine in some morbid states, 159.
  germs, cultures of, in ordinary Petri dishes in presence of air, 354.
Anaerobiosis, chemical criteria of, with special reference to methylene blue, 453.
  factors influencing, 454.
Anaesthesia, spinal, regional, and local, 516.
Analgesia, general, by cocaine injected into spinal theca, 522.
Anaphylactic bronchial asthma, 310.
  food reactions and eczema, 110.
  shock, influence of spleen, kidney, and thyroid on, 169.
  —, simple and harmless method of preventing, 458.
Anaphylaxis, blood picture in, 358.
  ocular reactions in, 164.
Aneurysm, arteriovenous, between carotid artery and cavernous sinus, 424.
  of carotid and vertebral arteries, 322.
Angina pectoris in diabetic patients, 499.
Angioma, gastric, 10.
Ankylostomiasis in coloured prisoners of war in Germany, 105.
  in Costa Rica, effects of treatment on, 106.
  in India, 106.
  in natives of Zaragoza, 107.
  in N. Queensland, 106.
  treatment of, 106, 107.
Annular ligament, incision of, in treatment of acute suppuration of wrist, 236.
Anoxaemia and cerebral activity, 430.
  effects of, on spinal reflex mechanism, 428.
  lactic acid in blood in, 376.
  in production of symptoms in disease and injury of nervous system, 427.
Anthelmintics, chemical composition and therapeutic value of, 106.
Anthrax, haemorrhagic meningo-encephalitis in, 161.
  infection in rats, experiments on, 161.
Antibody formation, effect of mustard gas on, 369.

Antiseptics, variability in results of testing, 465.
Anxiety hysteria, 349.
'Aolan' and turpentine, intramuscular injections of, in treatment of gonorrhoea, 214.
Aortitis, congenital syphilitic, 410.
  syphilitic, gastro-intestinal haemorrhage in, 11.
Appendix vermiformis, haemolytic streptococci of, 257.
  oxyuriasis of, 105.
Arsenic poisoning, magnesium sulphate in, 282.
Arsenical compounds in treatment of gonorrhoeal salpingitis, 216.
Arsphenamine, some factors relating to toxic action of, 580.
Arteries, injury causing spasmodic contraction of, 33.
Arthritis, chronic, bacteriologic studies in, 70.
  dysenteric, 400.
  gonorrhoeal, complicated by keratodermia blennorrhagica, 212.
Ascariasis, tongue sign in, 103.
Ascarides, intestinal obstruction caused by, 104.
  invasion of pancreas by, 104.
  — of lungs by, 104.
*Ascaris lumbricoides* causing haemolytic jaundice, 105.
  distribution and effects of, 104.
Ascites, chylous, due to carcinoma of stomach, 8.
  in connexion with duodenal ulcer, 5.
Aspergillosis, pulmonary, 317.
*Aspergillus fumigatus*, infection with, complicating influenza, 298.
Asphyxia, action of, on spinal animal, 429.
Asthma, bronchial, 310.
  —, treatment of, 312.
  vagotonia in, 312.
Asthmatics, anaphylactic deaths in, 311.
Auto-haemagglutination, 358.
Autolysin, bacterial, transmissible, 62.
Autolysis, effect of certain colloids upon, 86.
  microbic, transmissible, 74.
Auto-oxidizable constituent of the cell, 573.
Auto-suggestion, 244.

*Bacillus acidophilus*, intestinal implantation of, 90, 178.
  *anthracis*, action *in vitro* of neosalvarsan on, 458.
  *botulinus*, heat resistance of spores of, 352.
Bacillus carrier state, mechanism of, with special reference to Friedlaender bacillus, 467.
*Bacillus coli*, amount of heat liberated by, when grown in presence of free amino-acids, 567.
  — in intestine of small herbivora, 76.
  *influenzae*, accidental inoculation of, on mucous membranes of healthy persons with development of infection in at least one, 267.
  — antigens, complement fixation in influenza with, 155.
*Bacillus influenzae*, behaviour of, in mixed culture on haemoglobin-free media, 156.
  —, biology of, 58.
  —, grouping of, with special reference to permanence of type in carrier, 267.
  —, growth of, in haemoglobin-free media, 562.
  — isolated from meningitis, 561.
  —, nature of effect of blood-pigment upon growth of, 156.
  — pneumonia in monkeys, 153.
  —, production in monkeys of disease resembling influenza by inoculation with, 153.
  —, relation of different strains of, as shown by cross-agglutination and absorption tests, 155.
  —, serology of, 267.
  —, virulent, acute respiratory infection in man following inoculation with, 264.
  *leprae*, cultivation of, 558.
  *proteus*, biology and biochemistry of, 80.
  —, comparative studies on races of, with special reference to their capability to produce haemotoxin, 272.
  —, sub-groups of. Cross-agglutination as a differential diagnostic means, 272.
  — of war wounds, 451.
  *pyocyaneus*, bactericidal action of radium on, 187.
Bacillus of rabbit septicaemia, coexistence of individuals of different degrees of virulence in cultures of, 568.
*Bacillus spermoides*, a new anaerobic soil bacillus, 160.
  *typhosus*, viability and growth of, in bile, 79.
  *welchii* infections in dogs suffering from experimental diabetes, 273.
Bacilli, acid-resisting, changes shown by, on passing through animal organism, 452.
Bacteria, agglutination and sedimentation of, 176.
  communal activity of, 91.
  growth accessory substances in nutrition of, 387.
  *in vivo* as *in vitro*, pass through walls of filters, 255.
  simple procedure for accurate enumeration of, without use of counting chamber, 364.
Bacterial nutrition, studies on, 562.
Bactericidal action of secondary rays from colloidal metals, 94.
Bacteriology (abstracts), 57, 152, 255, 352, 450, 550.
Bacteriophage, d'Herelle's, production and interpretation of, 62.
  presence of, in healthy intestine, in soil and in water, 74.
Bacteriophagic microbe, 74.
  principle of d'Herelle, 74.
*Bacterium pneumosintes*, 561.
Basal ganglia, mental disturbances in tumours of, 447.
Behring's toxin-antitoxin mixture, practical protective value of, against diphtheria, 454.
Benzidin peroxidase reaction, variations in, depending on fixative, physiological activity, and type of animal, 68.

Benzyl benzoate in treatment of dysentery, 404.
  — in treatment of whooping cough, 203.
Bile-duct, surgical union of, with duodenum, jejunum, or stomach, 131.
  cancer of, 129.
  kinking of, 128.
Bile-ducts, congenital obliteration of, 127.
Bile enemata in treatment of constipation, 15.
Bile salts, effects of, on respiration, 383.
  influence of, on gastric function, 465.
Biliary obstruction not due to gall-stones, 127.
  surgery, 125.
Biochemistry (abstracts), 84, 173, 273, 376, 468, 573.
Blackwater fever, 457.
Bladder, diverticula of, 184.
Blood after administration of urea, 277.
  alkaline reserve of, in the insane, 277.
  — —, changes in, in experimental infections, 368.
  appearance and distribution of fats and lipoids in, after bleeding, 376.
  carbon dioxide carriers of, 379.
  coagulation of, rôle of calcium in, 558.
  — theories of, 550.
  concentration of lactic acid in, in anoxaemia and shock, 376.
  corpuscles, chemical composition of, 579.
  — and plasma, distribution of phosphates between, 469.
  —, permeability of, to sugar, 86.
  —, red, diurnal variation in size of, 366.
  —, —, influence of certain digitalis bodies on permeability to ions of, 174.
  —, —, isoelectric point of, and its relation to agglutination, 176.
  —, —, and outer fluid, distribution of glucose between, 471.
  —, —, rate of sedimentation of, 175.
  —, —, rate of sedimentation of, during pregnancy, 543.
  —, —, structure of, 367.
  —, —, volume of, and ratio of this volume to haemoglobin and to number of cells, 365.
  —, sedimentation of, 377.
  —, simple procedure for accurate enumeration of, without use of counting chamber, 364.
  count of normal monkeys, 572.
  —, white, of glycosurics, effect of glucose on, 498.
  counts, Bürker's method for, 277.
  cultures, interpretation of, 458.
  diastases in, source of, 469.
  diastatic ferments of, 87.
  diseases, classification of, 118
  distribution of chlorides in, 88.
  of dogfish, sand-shark, frog, and pigeon, sugar in, 471–2.
  effect on the composition of, of maintaining an increased blood-volume by intravenous injection of gum acacia in normal, asphyxiated, and shocked dogs, 273.
  — of sweating and diuretics on, with diet rich and poor in salt, 575.
  — of surgical anaesthesia on reaction of, 67.
  fat constituents of rabbit, variation of, 88.
Blood, fate of india ink injected into, 171.
  ferment, studies of, in pregnancy, carcinoma, and pulmonary tuberculosis, 162.
  groups, distribution of, in patients suffering from 'malignant disease', 461.
  human, carbon dioxide dissociation curve and arterial and venous carbon dioxide tension of, in health and disease, 173.
  paradoxical hyperalbuminosis in, of cancer subjects, 466.
  phosphates in lipaemia produced by acute experimental anaemia in rabbits, 174.
  as a physico-chemical system, 469.
  picture in typhus, 196.
  — in whooping-cough, 202.
  pressure estimation by indirect methods, 378.
  —, action of irradiation on, 278.
  —, arterial, measurement of, in horses, 279.
  —, capillary, in man, measurement of, 166.
  sugar regulation and origin of hyperglycaemias, 470.
  — in diabetes, 502.
  —, physiology of, 377.
  — tolerance in gastro-intestinal carcinoma, 8.
  suspension stability of, in pulmonary tuberculosis, 366.
  use of Romanowsky type of stain for, 364.
  vessels, experimental studies of properties of surviving, under treatment with chemical stimuli, 378.
  volume, influence of injections of acacia-glucose solutions on, 277.
Body-weight, effect of sweating and diuretics on, with diet rich and poor in salt, 575.
Bone-marrow of rats exposed to $\gamma$ radiations from radium, histological changes in, 93.
Bones, experimental investigations on influence of mechanical compression on, 369.
Bothriocephalus anaemia, 108.
*Bothriocephalus*, complement fixation by the hosts of, 163.
Botulism from cheese, 353.
Brachial plexus, anaesthesia of, 525.
Brain, basal arteries of, and their functional significance, 348.
  blood supply to, 323.
  chemical composition of, in dementia praecox, 479.
  tumour, superficial, 446.
  volume, experimental production of alterations in, 535.
Bronchitis, fibrinous, 312.
Bulbo-pontine syndrome in typhus, 195.
Bürker's method for blood counts, 277.
Butter, effect of heat and oxygen on nutritive value of, 84.

C. L. P. (malum coxae Calvé-Legg-Perthes), 40.
Caecum, plication of, in treatment of constipation, 227.
Calcium combination with animal tissues, 478.
Calomel, purgative action of, 180.
Calorimetric investigations on inanition and deficiency disease, 167.

Cancer, abdominal, size of spleen in, 120.
  of bile-duct, 129.
  of breast, treatment of, by excision supplemented by radiation, statistics relating to, 418.
  of cervix, radium therapy of, 392, 584
  grafts, effect of cellular reaction induced by X-rays on, 488.
  inoculation, influence of, on lymphoid stimulation induced by small doses of X-rays, 489.
  melanotic, 229.
  —, structure of, 233.
  of oesophagus treated by direct application of tube of radium emanation to oesophageal wall through the transpleural channel, 284.
  patients, distribution of blood groups in, 461.
  paradoxical hyperalbuminosis of blood in, 466.
  primary, of lung, 317.
  relation between time and extent of lymphoid stimulation induced by physical agents and degree of resistance to, in mice, 489.
  of stomach, 7.
  —, methods of diagnosis of, 92.
  transplanted, effect of small doses of X-rays of low penetration on the resistance of mice to, 489.
  *see also* names of particular forms of.
Capillaries, functional activity of, 278.
Capillary blood-pressure in man, measurement of, 166.
Caramel in treatment of diabetes, 506.
Carbohydrate metabolism and diabetes, 86.
  — of isolated amphibian muscle, 577.
Carbolic acid, use of, for isolating pathogenic bacteria from material contaminated with *B. proteus*, 80.
Carbon dioxide absorption curve and carbon dioxide tension in blood of normal resting individuals, in cardiac dyspnoea, and in severe anaemia, 381.
  carriers of blood, 379.
  dissociation curve and arterial and venous carbon dioxide tension of human blood in health and in disease, 173.
Carbon monoxide poisoning, 430.
Carcinoma, blood ferment in, 162.
  of pancreas, 512.
Cardia, Röntgen observations on anatomy and physiology of, 388.
Cardiac dyspnoea, carbon dioxide absorption curve and carbon dioxide tension in, 381.
  respiratory mechanism in, 382.
Cardiospasm, impermeable, treatment of, 15.
Carotid artery, 322.
  arteriovenous aneurysm between, and cavernous sinus, 424.
Cataract, action of radium in, 285.
Cavernous sinus, arteriovenous aneurysm between, and carotid, 424.
Cell, auto-oxidizable constituent of, 573.
  new experiments on uptake of substances by, 478.
Cerebral metabolism, 476.
Cerebral softening from metallic embolus in left middle cerebral artery, 251.
  thrombosis and embolism, 322.
  tumours, localization or elimination of, by ventriculography, 182.
Cerebrospinal fluid, constitution of, deciding factor for prognosis and therapy in syphilis of nervous system, 59.
  in syphilis, 336.
  general colloid test in, and use of Congo-rubin, 479.
  pressure, experimental alterations in, 535.
  in typhus, 195.
  in whooping-cough, 202.
Chancroid, 218.
Chaulmoogra oil, influence of, on tubercle bacillus, 262.
Chloral hydrate solution, gargling with, in treatment of influenza, 305.
Chloroma, colouring matter in, 579.
Cholecystectomy, mortality from, 126.
Cholecystitis, 127, 128.
Cholesterol content of serum, variation in, in pneumonia, 87.
Choline, hormone of intestinal peristalsis, 479.
Chorionic ferments causing spirillolysis, 407.
Cicatrices, deformities of hands since childhood caused by, 482.
Citrus fruit juices, fresh, determination of minimum doses of, which will protect a guinea-pig from scurvy, together with some observations on preservation of such juices, 386.
Climatological studies: active factor in high altitudes, 278.
Cobra venom, immunity to, 360.
Cocaine injections, danger of, 519.
  into spinal theca, general analgesia by, 522.
Cod-liver oil, effect of, on experimental rickets in rats, 176.
Codein derivatives, acclimatization to, 180.
Colds, bacteriology of, 267.
Colectomy, 223.
Colitis, membranous, in influenza, 299.
  ulcerative, a sequel to bacillary dysentery, 401.
Colloidal metals, bactericidal action of secondary rays from, 94.
  nutrient solutions, importance of, for normal, exhausted, and poisoned heart, 576.
Colloids, influence of, on non-colloidal drugs, 282.
Colon, symptoms due to extreme elongation and dilatation of, 14.
Complement fixation by the hosts of *Bothriocephalus*, 163.
  test for gonorrhoea, 212.
Congo-rubin, use of, 479.
Constipation treated by bile enemata, 15.
Coolidge tube, danger of, for screen work, 394.
Coxalgia, non-tuberculous juvenile, 38.
Creatinin excretion, course of, in urine of man, with especial reference to effect of exercise, 180.
Creatinuria of man, diet and sex as factors in, 469.
Cryotherapy, 114.
Cylindromata of facial region, 467.

Cyst of common bile-duct, 128.
Cystic pneumatosis of intestine, 6.
Cystin, oxidation of, by blood charcoal, 480.
Cystitis after typhus, 196.
Cutaneous sensibility, semeiological importance of electrical examination of, 490.
Cutex verticis gyrata, 114.

Deafness due to congenital syphilis, 411.
Decerebrate rigidity in man and occurrence of tonic fits, 55.
Deficiency disease, calorimetric investigations on; 167.
Dementia praecox, chemical composition of brain in, 479.
Dermatitis due to handling figs infected with the mite *Carpoglyphus passularum*, 113.
  X-ray, followed by heat dermatitis, 391.
Dermatosis, precancerous, 114.
Diabetes, experimental, *B. welchii* infection in, 275.
  —, influence of cold in, 276.
  —, influence of extreme age on production of, 276.
  —, influence of fever and intoxication in, 275.
  —, influence of pregnancy on, 281.
  —, studies in, 273.
  mellitus, 497.
  —, aetiology of, 497.
  blood-sugar in, 502.
  and carbohydrate metabolism, 86.
  frequency of, in U.S.A., 498.
  and hirsuties, 502.
  and leukaemia, 501.
  mortality from, 498.
  pancreatic, relation of alkali reserve of blood to glycosuria and hyperglycaemia in, 173.
  and pregnancy, 501.
  prophylaxis of, 503.
  renal, 502.
  surgical complications of, 500.
  symptomatology of, 498.
  treatment of, 504.
  and tuberculosis, 500.
Diabetic urine, acetaldehyde in, 576.
Diarrhoea, infantile, 12.
Diastatic ferments of blood, 87.
Diathermy in treatment of whooping-cough, 203.
Dicotyledonous plant, infection with, causing Recklinghausen's disease, adenoma sebaceum, and tuberous sclerosis, 114.
Diet and growth, 386, 387.
Digestive tract, atonic syndrome of, in nervous persons, 389.
Digitalis bodies, influence of certain, on permeability to ions of human red blood corpuscles, 174.
Diphtheria, 18.
  aetiology of, 18.
  carriers and their treatment with mercurochrome, 454.
  diagnosis of, 24.
  epidemiology of, 18.
  immunity from, 26.
Diphtheria infections with particular reference to carriers and to wound infections with *B. diphtheriae*, 454.
  of middle ear, 19.
  of mouth, 19.
  in the new-born, 21.
  prophylaxis of, 25.
  symptomatology of, 19.
  treatment of, 27.
  of umbilicus, 20.
  of vulva, 20.
  wound, 23.
  —, bacteriology of, 162.
  —, chemotherapeutic experiments with a view to treatment of, 355.
Diphtheritic paralysis, 24.
Disodiumphosphate as a catalyst for quantitative oxidation of glucose to carbon dioxide with hydrogen peroxide, 178.
Disseminated sclerosis, aetiology of, 149.
  experimental investigations on pathogenesis of, 347.
  unusual motor symptoms in, with reference to differential diagnosis from epidemic encephalitis, 248.
'Dopa' test for tyrosinase, 230.
Drigalski-Conradi, influence of nutrose in culture medium of, 77.
Drugs, acclimatization to. Acclimatization to codein derivatives (eucodal and paracodein), 180.
Duodenal diverticula: their clinical and radiological aspects, 183.
  perforation treated by duodenal alimentation, 15.
  ulcer, 4.
Dupuytren's contraction, 52.
Dysenteric arthritis, 400.
  forms, mixed, 456.
Dysenteriform catarrh due to flagellata, 399.
Dysentery, 399.
  aetiology of, 399.
  amoebic, 402.
  bacillary, studies on epidemic of, 456.
  —, aetiology of, 272.
  —, sero-diagnosis in, 456.
  —, in dog with simultaneous schistosomiasis, ankylostomiasis, and filariasis, 79.
  bacilli, divisions of Flexner group of, 77.
  bacteriology of, 57.
  in children, 400.
  diagnosis of, 403.
  epidemiology of, 399.
  gastric and pancreatic secretions in, 401.
  historical, 399.
  prognosis of, 403.
  protozoan, epidemiological, and clinical notes on, 456.
  symptomatology of, 400.
  treatment of, 403.

Eclampsia, biochemistry of, 537.
Eczema, aetiology and treatment of, 110.
Eichloff-blue, use of, for isolating pathogenic bacteria from material contaminated with *B. proteus*, 80.
Elbow, anterior dislocation at, 41.
Electric currents, action of, on endocrine glands and other tissues, 99.

Electric currents, high-frequency, plethysmographic investigations on effects of, 279.
  mode of death by, 587.
Electro-diagnosis (abstracts), 490.
Electromyogram in nervous diseases, 530.
Electroradiology in neuritis of motor nerves, 492.
Electrotechnique (abstracts), 587.
Electrotherapy (abstracts), 99, 492.
Elsner's gastroscopy, practical value of, 439.
Embolism, cerebral, 322.
Emerods, 399.
Empyema, experimental streptococcus, 69.
Encephalitis, haemorrhagic, as complication of dysentery, 402.
  lethargica, differential diagnosis of, from disseminated sclerosis, 248.
  —, experimental study of, 148, 262.
  —, experimental, transmission of, 65.
  —, following typhus, 195.
  —, microscopic observations on brains from some cases of, 452.
  —, psychiatric aspects of, 447.
  —, special microscopic finding in nervous tissue from cases of, 452.
  —, treatment of medullary and radical after-effects of, 493.
  —, winter incidence of, and seasonal recurrence of chronic forms, 57.
  neonatorum, 253.
  and polyomyelitis, immunological distinctions of, 263.
Endocrine glands, action of electric currents on, 99.
Endothelial reactions in tuberculosis, 375.
Endotheliomata of nasopharynx, 243.
*Entamoeba macrohyalina*, 457.
Enteritis, acute infectious, complicated by polyneuritis, 12.
Enterococcus, properties and relations of, 257.
Enterostomy for post-operative intestinal obstruction, 440.
Enzymes, proteoclastic, in normal and pathological urine, 385.
Eosinophilia in sputum in asthma, 311.
Epilepsy, diabetic, 499.
  following gun-shot wounds of skull, pathology of, 448.
Epithelioma adenoides cysticum (Brooke) or tricho-epithelioma papillosum multiplex (Jarisch), 464.
  of skin, 114.
Erythrocytes: *see* blood corpuscles, red.
Erythromelalgia, 113.
Ether, intramuscular injection of, in treatment of whooping-cough, 202.
Eustachian tube, intracranial extension of sarcomata of, 242.
Evolution, neural, aspects of, 50.
Exophthalmos, pulsating, treated by ligature of both common carotids, 426.
Eye diseases due to congenital syphilis, 411.
  melanoma and melanotic cancer of, 234.
  simplified technique for radiotherapy of, 583.
Eyes, tonic labyrinthine and neck reflexes of, 151.

Fat, animal, effect on kittens of a diet deficient in, 386.
  content of embryonic livers, 88.
Fats, action of ozone on fat-soluble factor in, 85.
  growth and nutrition on diets free from, 177, 178.
Fibrinolysis, 282.
Fibroid, pregnancy after radiotherapy for, 95.
Fibroids, uterine, radium therapy for, 285.
Fibromyoma tissue, chemical analysis of, 280.
Fibromyomata of uterus, intensive X-ray therapy versus hysterectomy for, 95.
Flea-bites, liability of diabetics to, 500.
Flexner group of dysentery bacilli, divisions of, 77.
Flies, action of, in spread of dysentery, 399.
Fontan's method of treating chancroidal buboes, 220.
Foods, analyses and energy values of, 573.
Friedberger-van-der-Reis skin reaction in diagnosis of typhus, 197.
Friedmann's tortoise bacilli, antigenic action of, 261.

Gall-bladder, anatomy and physiology of, 126.
Gall-bladders, pathological changes in 4,998 removed, 126.
Gall-stones, formation of, and detection by X-rays, 127.
  study of, by X-rays, 92.
*Galleria mellonella*, immunity, natural and acquired, in larva of, 82.
Gangrenous infections of animals, aetiology of acute: a discussion of blackleg, braxy, malignant oedema, and whale septicaemia, 160.
Gas cysts of abdomen, 10.
  phlegmon following subcutaneous injections, 568.
Gasoline vapour, anaesthetic and convulsant effects of, 280.
Gastric analysis, 3, 474.
  angioma, 10.
  function, influence of bile salts on, 465.
  myomata, 10.
  polyposis, 9.
  and respiratory response to meals, 466.
  secretion and motility, effects of restricted (so-called ulcer) diets on, 15.
  secretions in bacillary dysentery, 401.
  — in starvation, 473.
  ulcer, 4.
  *see also* stomach.
Gastrin, response of stomach glands to, before and shortly after birth, 474.
Gastro-intestinal haemorrhage, 11.
  tract, X-ray interpretation of, 389.
Gastroscopy, Elsner's, 439.
Gastrospasm, reflex, 129.
Gaucher's disease, 119, 170.
Gentian violet reaction, 91.
Giant cells in cultures from human lymph nodes, 370.
Gigantism, experimental production of, by feeding anterior lobe of hypophysis and pituitary gland, 179.

Globin, antigenic properties of, with a note on the independence of properties of serum and tissue proteins as exemplified by absence of antibody from globin of an immunized animal, 165.
Glycaemia, adrenalin, 576.
Glycogenic infiltration of liver of laboratory rabbits, 67.
Glycosuria, association of, with infectious diseases, 497.
Gonococcal infections of the heart, 211.
  septicaemia, 210.
Gonococci, serological investigations on, 450.
*Gonococcus*, growth of, in various gaseous environments, 256.
  relative toxicity of different strains of, 210.
  types of, 157, 257.
Gonorrhoea, 210
  aetiology of, 210.
  chronic, in women, comparison of smear, culture and complement fixation, 157.
  diagnosis of, 212.
  in the female, 214.
  prostitution and alcohol in causation of, 210.
  symptomatology of, 210.
  treatment of, 214.
Gout, roentgenographic studies in, 484.
Grafts of dead tendon, 527.
Gram reaction, parallelism between, and gentian violet reaction, 91.
Graves's disease, 341.
  use of radiotherapy in, 390.
  thyroid lesions in, 247.
Growth on diets poor in true fats, 177.
Growth-promoting properties, comparison of, for guinea-pigs, of certain diets consisting of natural foodstuffs, 386.
Gum acacia injections, temperature changes induced by, in normal and fevered animals, 90.

Haemagglutination, its medico-legal bearing, with observations upon the theory of isoagglutinins, 163.
Haematology, employment of complex stains based on Romanowsky principle in, 364.
Haemato-respiratory functions. An irreversible alteration of $H_2CO_3$/$NaHCO_3$ equilibrium of blood induced by temporary exposure to a low tension of $CO_2$, 174.
Haemoglobin, reduced, light absorption of, 376.
  variable acidity of, 88.
Haemolysin, anti-human, production of, with special reference to immunization with erythrocytes sensitized with heated serum, 165.
Haemolysis, 367.
Haemolytic sensitizer and red blood corpuscles, equilibrium between, in relation to H-ion concentration, 378.
Haemophilic bacilli, biological study of, 154.
Haemorrhage following acute septic infection, 325.
  following removal of tonsils, 326.
Haemorrhage from carotid and vertebral arteries following gunshot wounds, 328.
  reactions to, 470.
Haemotoxin of streptococci, biological and physical properties of, 69.
Hay fever, aetiology and treatment of, 309.
Heart, effects of warming and cooling sino-auricular node in, 472.
  failure in diphtheria, 23.
  fibrillation of, 472.
  gonococcal infections of, 211.
  isolated, frog's, effects of some chlorine derivatives of methane, ethane, and ethylene on, 472.
  perfused, researches on, 280.
Heat regulation of mammals, chemical, 378.
Hemiplegia following ligature of common carotid, 324.
  following tonsillectomy, 327.
  pleuritic, 319.
Hepatic function in eclampsia, 539.
'd'Herelle phenomenon,' some peculiarities of, 74.
d'Herelle's bacteriophage, 74.
  bacteriophage, production and interpretation of, 62.
Hernia, superficial inguinal, 241.
Hernias, large umbilical and ventral, treatment of, 239.
Herpes, virus of, 451.
  zoster, 112.
Hibernation, artifical, in mice, 378.
Hirsuties in diabetics, 502.
Histamin, action of, on man, 580.
Honey, vitamine content of, 468.
Hookworm infection : *see* ankylostomiasis.
Hydatid cysts of kidney, pyelography in diagnosis of, 287.
Hydrocephalus due to occlusion of foramina of Magendie and Luschka, diagnosis and treatment of, 549.
Hydrogen electrode, probable error in determinations by means of, 255.
Hydrogen-ion concentration of broth media, variations in, 566.
  equilibrium between haemolytic sensitizer and red blood cells in relation to, 378.
  relation of, to growth, viability, and fermentative activity of *Streptococcus haemolyticus*, 565.
Hyperacidity, 4.
Hyperglycaemia, difference between the mechanism of production of, by ether and chloroform, 274.
Hyperglycaemias, origin of, 470.
Hypertrichosis, electrolysis treatment of, 114.
Hypophysis, anterior lobe of, experimental gigantism produced by feeding, 179.
  radiotherapy of tumours of, 582.
  treatment of tumours of, by actinotherapy, 486.
Hypopyon complicating typhus, 196.
Hysteria, anxiety, 349.

Icterus neonatorum, breaking down of maternal blood as cause of, 580.
Ileo-sigmoidostomy, 140.
Immune bodies, specific, transmission of, from mother to young, 164.

Immunity to cobra venom, natural and acquired, 360.
  natural and acquired, in larva of *Galleria mellonella*, 82.
Inanition. calorimetric investigations on, 167.
Induction coils, action of, 181.
Infants' foods, digestion of, 387.
Influenza, 295.
  aetiology of, 155. 296, 563.
  — : experiments in search of filter-passing virus, 66.
  association of with whooping-cough, 201.
  bacillus : *see B. influenzae.*
  bacteriology of, 267, 562.
  blood in, 296.
  in children, 303.
  chronic lung disease following, 297.
  and common colds, attempt to cultivate filterable viruses from, 264.
  disease resembling, produced in monkeys by inoculation with *B. influenzae*, 153.
  epidemiology of, 295.
  immunity against, 303.
  nervous and mental complications of, 299.
  in old age, 303.
  pathology of, 264, 562.
  prophylaxis of, 304.
  renal complications of, 299.
  skin in, 300.
  studies of the nasopharyngeal secretions from patients, 266, 560.
  surgical complications of, 300.
  symptomatology of, 297.
  and syphilis, 302.
  transmitted through fleas, 296.
  treatment of, 305.
  and tuberculosis, 301.
  vaccination against, 564.
Integrative action of nervous system, 144.
'Intertraction' between albuminous substances and saline solutions, 577.
Intestinal exclusion, 137.
  infection, non-specific, 12.
  obstruction caused by ascarides, 104.
  —, post-operative, enterostomy for, 440.
  parasites, 103.
  —, frequency in young children, 103.
  stasis, chronic, surgical treatment of, 221.
Intestine, the anaerobic flora in some morbid states of, 159.
  fate of micro-organisms introduced into isolated loops of, 79.
  large, results of operations for atony and prolapse of, 223.
  of small herbivora, flora of, 76.
Intracranial tension, alteration of, by salt solution in alimentary canal, 178.
Iodine, biochemistry of: comparative effects of thyroid and iodide feeding on growth in white rats and in rabbits, 179.
  compounds, specific, influence of, upon metamorphosis of frog's larvae and axolotl, 578.
Ipecac. sensitization and bronchial asthma, 310.

von Jaksch syndrome, 119.
Jaundice complicating gonococcal septicaemia, 211.
  haemolytic, 122.
  —, caused by *Ascaris lumbricoides*, 105.
  in influenza, 299.
  occurring after revaccination in adults, 209.

Keratin, composition of, 110.
Keratodermia blenorrhagica, complicating chronic gonorrhoeal arthritis, 212.
  a form of psoriasis, 110.
Kidney, pyelography in diagnosis of hydatid cysts of, 287.
Kidneys, radiological examination of, after intraperitoneal insufflation, 286.
Knee-jerk, relation of form of, to muscle tonus, 54.
Köhler's disease, 483.
  with special reference to its aetiology, 345.

Labyrinthine reflexes to progressive movements, 151.
Lactation, influence of, on sexual cycle in rat and guinea-pig, 475.
Lactic acid in blood in anoxaemia and shock, 376.
Lard, nutritive value of, 85.
Larynx, treatment of cancer of, by local applications of radium, 285.
Lecithin of brain, 473.
Leiomyoma of smooth muscle-cells of arrectores pili, 114.
Leprosy, histopathology of, 372.
Leuco-agglutinins, 461.
Leucocytes, changes in, in experimental infections, 368.
Leucocytic exudates and transmissible bacterial autolysin, 62.
  formula, normal, 169.
Leucocytolysis produced by röntgenization of spleen, treatment of infectious diseases by, 485.
  chemotactic effect of osmosis upon, 362.
Leukaemia, action of X-rays in, 486.
  acute, in pregnancy, 64.
  and diabetes, 501.
  transmissible, new strain in fowls (strain H), 572.
Leukoplacia treated with carbon dioxide snow, 114.
Lice, importance of, in transmission of typhus, 194.
Lichen and lichenification, 111.
Light baths, universal, in treatment of eye diseases, 346.
Linitis, plastic, 4.
Lipaemia in acute anaemia, 88.
  chemistry of, 376.
Lipoid granules, special staining method for, in nerve-cells, 252.
Liver, artificially perfused, experiments with antigens and antibodies upon surviving, 388.
  composition of, in acute yellow atrophy, 479.
Luetin reaction, value of, in diagnosis of congenital syphilis, 412.

Lumbago, origin and symptomatology of, 349.
Lumbar puncture, troubles due to, 521.
Lung, congenital absence of, 309.
  chronic disease of, following influenza, 297.
  gangrene of, 316.
  infection, non-tuberculous, 313.
  new growths of, 317.
  *see also* pulmonary.
Lupus erythematosus, 112.
  vulgaris, treatment of, with liquid acid nitrate of mercury, 112.
Lymphadenoma with pruritus, 114.
Lymphocytes, fate of, 572.

Malta fever, prophylactic vaccination against, 256.
Mammary gland, lactating, effect of suckling and castration on, in rat and guinea-pig, 474.
  secretion, effect of diet on, 387.
Manchester and district Radium Institute, report of, 283.
Measles, experimental, symptomatology and pathology of, in monkeys, 354.
  susceptibility of monkeys to, 354.
Media, influence of reaction of, and of presence of buffer salts on metabolism of bacteria, 66.
  reaction of, 564.
Melanin, 229.
Melanoblastoma, 229.
Melanogen in urine, 229.
Melanoma, 229.
  structure of, 233.
Memorial Hospital, New York, radium technique at, 290.
Ménière's disease, symptoms of, complicating influenza, 301.
Meningitis, serous, post-traumatic, in children, 253.
Meningococcal infection, certain problems concerning, 258.
Meningococci, serological investigations on, 450.
*Meningococcus*: experimental studies of mode of action of antimeningococcal serum, 63.
  production of antimeningococcic serum, 81, 82.
Meningo-encephalitis, haemorrhagic, in anthrax, 161.
Mercurochrome in treatment of diphtheria carriers, 454.
Mesothelioma of pleura, 319.
Metabolism, bacterial, 90.
  general water, secretion of water by kidney in relation to, 575.
Methylene blue in treatment of gonorrhoea in women, 216.
Microbic species, dissociation of, 568.
Milk, condensed, full cream, sweetened, investigation of antiscorbutic value of, by experiments on monkeys, 387.
  deficiency of heat-treated, 85.
  dried, antiscorbutic value of, 387.
  influence of diet of cow upon nutritive and antiscorbutic properties of, 177.
  powders, antiscorbutic potency of, 468.
Milk, vitamine content of, 84.
Morgan's bacillus, 271.
Motor system, extrapyramidal, organization of, 443.
Multiple sclerosis and psycho-analysis, 441.
Muscle, carbohydrate metabolism of isolated amphibian, 577.
  influence of subminimal stimuli upon course of chemical changes in, 577.
  tone, nature of, 532.
Mustard gas, effect of, on antibod , 369.
  effect of, on experimental tuberculosis, 369.
Myelitis in dysentery patient, 402.
Myeloma of spine, 250.
Myiasis cured by excision, 114.
Myocardial involvement, post influenzal, 298.
Myomata, gastric, 10.

Naevus derived from branchial clefts, 114.
  warty, in heredo-syphilitic subject, 410.
*Necator americanus* in India, 106.
Neosalvarsan, splenomegaly following injection of, 122.
  in treatment of congenital syphilis, 414.
Nerve-cells of parietal plexuses of gastro-enteric canal, lesions of, in consequence of surgical interventions, 371.
  lesions in early syphilis and their treatment, 61.
  and plasmodesma, 445.
  regeneration, 351.
  root fibres, posterior, intramedullary bifurcation of, in man, 549.
  section in man, experimental, results of, 46.
  tissue, cultivation of, 351.
Nervous diseases, electromyogram in, 530.
  system, dissolution of function in disease of, 141.
  —, elementary, physiology of, 141.
  —, insulation of, 48.
  and mental complications of influenza, 299.
Neuritis of motor nerves, electroradiology in, 492.
Neuroglia fibres, quick process for staining, 168.
Neurology (abstracts), 53, 146, 242, 347, 441, 547.
Neurosyphilis, 335.
  constitution of cerebrospinal fluid in prognosis of, 59, 60.
  increased incidence of, 335.
  intraspinal treatment of, 338.
  prognosis and therapy of, 59, 60.
  relation of, to previous treatment, 335.
Novarsenobenzol in treatment of congenital syphilis, 416.
  — of diabetes, 506.
Novocaine and bicarbonate solution, toxic effects of injection of, into a vein, 518.
  as local anaesthetic, disadvantages of, 520.
Nutrition, 468.
  in diets practically devoid of fat, 178.
Nutrose, influence of, in culture medium of Drigalski-Conradi, 77.

Obesity preceding diabetes, 503.

- Oculo-cardiac reflex (Dagnini-Aschner phenomenon)—its use in medicine and psychology, 150.
- Oesophagus, treatment of cancer of, by local applications of radium, 285.
- Oils, hydrogenated, digestibility of, 282.
- Oleic acid and trioleins, haemolytic action of, in rabbits, 166.
- Onychodystrophy following typhus, 195.
- Opacity of liquids, methods of measuring, 580.
- Ophthalmia and diet, 574.
- Ophthalmology, universal light baths in, 346.
- Orchilytic sera, sexual neutralization obtained by means of, 169.
- Oriental sore, treatment of, with X-rays, 114.
- Osmosis, chemotactic effect of, on leucocytosis, 362.
  - as factor in local accumulation of leucocytes in body, 90.
- Osteo-arthropathy, hypertrophic pulmonary, following lung abscess, 315.
- Osteochondritis deformans juvenilis, 39.
  - of upper epiphysis of femur, 39, 481.
- Osteolysis, 372.
- Osteo-myelitis of hyoid after influenza, 301.
- Otoliths, functions of, 152.
- Ovariolytic sera, sexual neutralization obtained by means of, 169.
- Oxalic acid, determination of, in urine and faeces, 473.
- Oxaluric acid, determination of, in urine and faeces, 473.
- Oxygen administration, effects of, in decerebrate cats, 383.
  - low, effects during rebreathing, 382.
  - subcutaneous injections of in treatment of influenzal broncho-pneumonia, 305.
- Oxyuriasis, tongue sign in, 103.
  - of vermiform appendix, 105.
- *Oxyuris vermicularis*, prevalence of, due to war, 105.

- Paget's disease, extra-mammary, 114.
- Pain, frequency of, 44.
  - functional value of, 44.
  - physiology of, 43.
  - relation of, to bodily cause, 44.
  - —, to other forms of sensation, 50.
  - sensibility to, in skin, 45.
- Pancreas, annular, 509.
  - atrophy of, 511.
  - carcinoma of, 512.
  - cirrhosis of, 511.
  - diseases of, 509.
  - —, diagnosis of, 514.
  - necrosis of, 510.
  - syphilis of, 511.
- Pancreatic achylia or hypochylia, 511.
  - calculi, 513.
  - secretions in bacillary dysentery, 401.
- Pancreatitis, chronic, 510.
- Pangenesis, 74.
- Paragglutination, 355.
- Paralyses of pyramidal origin, selective incidence of, 443.
- Paralysis, diphtheritic, 24.
- Para-meningococci, serological investigations on, 450.
- Paraoxyphenylacetic acid, formation of, from laevo-tyrosin by bacteria, 473.
- Paraoxyphenylacrylic acid, formation of, from laevo-tyrosin by bacteria, 473.
- Parathyroid secretion, stability of nervous system as factor in resistance of albino rat to loss of, 475.
  - tetany, relation between, and calcium deficit in blood, 278.
- Paratyphoid B bacillus related to rodent group, spontaneous epidemic among laboratory rabbits caused by, 80.
- Paravertebral injections, 523.
- Parosmia, 281.
- Parotid swelling due to denture, 3.
- Patellar clonus, relation of, to muscle tonus, 54.
- Pathology (abstracts), 57, 152, 255, 352, 450, 550.
- Pellagra, 113.
  - sulphocyanate content of saliva and urine in, 283.
- Pericolitis membranacea, 226.
- Periodic breathing of decerebrate cats, 383.
- Periodicity of gastric ulcer, 6.
- Peripheral nerves, insulation of, 49.
- Perspiration, insensible, through cutaneous scars and skin of paretic limbs, 370.
- Petro-sphenoidal junction, syndrome of, 242.
- Phagedaena, development of, in vaccine pustule, 208.
- Phagocytes, mononuclear, of lung, experimental study of, 462.
- Phagocytosis, action of certain salts on, 361.
  - experimental investigations on, influence of various fixing agents, fatigue and diluted solutions of HCl, 171.
  - investigations on, 460.
  - of solid particles, 478.
- Phenolic substances, estimation of, in urine, 86.
- Phenolphthalein, purgative action of, 180.
- Phosgene poisoning, experimental pathology and therapy of, 384.
- Phosphates, distribution of, between blood-corpuscles and plasma *in vivo* and *in vitro*, 469.
- Physical exertion, fitness, and breathing, 280.
- Pilomotor reflex, 246.
- Pituitary body, secretory activity of anterior lobe of, during pregnancy, 371.
  - gland, experimental gigantism produced by feeding, 179.
  - opotherapy of diabetes, 507.
- Plague, experimental investigations on immunity of rats against, 459.
  - complement fixation test for diagnosis of, 361.
  - means of importation of, into Italy and preventive measures, 459.
- Plasmodesma and nerve, 445.
- Pleura, new growths of, 319.
  - removal of particulate matter from, 462.
- Pleural effusions, encapsuled, radiological appearances of, 581.
- Pleurisy, mediastinal, 318.
  - parabronchial, 318.

Pleuritic hemiplegia, 319.
Plumbism causing gastric ulcer, 5.
Pneumatosis, intestinal, 10.
Pneumobacillus causing pulmonary abscess, 315.
Pneumococci from the upper respiratory tract, serological relationships of, with special reference to common colds and influenzal conditions, 267.
  types of, 73.
*Pneumococcus*, enzymes of, 71.
Pneumonia, experimental, 153.
  influenzal, pathological-anatomical and bacteriological study of, 562.
  variation of cholesterol content of serum in, 87.
Pneumonomycosis aspergillina after influenza, 298.
Pneumothorax, experimental and critical studies on, 570.
  determination of volume of pleural cavity in course of, 571.
  spontaneous, 319.
Poliomyelitis, acute, 146.
  and encephalitis, immunological distinctions of, 263.
  transient, following influenza, 300.
Polycythaemia hypertonica, gastro-intestinal haemorrhage in, 11.
  radiotherapy of, 390.
Polyposis, gastric, 9.
Precipitin response in blood of rabbits following subarachnoid injections of horse serum, 569.
  test for gonorrhoea, 213.
Pregnancy after radiotherapy for fibroid, 95.
  ammonia coefficient of, 89.
  blood ferment in, 162.
  and diabetes, 501.
  toxaemias of, 537.
Pressure, low, physiological effects of short exposures to, 174.
Protein meal given to a man at end of 8-day fast, effect of, 86.
  non-specific, in treatment of gonorrhoeal arthritis, 214.
  production of fat from, 86.
  racemization, comparative investigation of corresponding proteins of cow and ox serum, cow's colostrum and cow's milk by method of, 575.
Proteinogenous amines, biological effect of, 578.
'Protopathic' animal, 142.
Pseudo-ascites in children, 13.
Pseudo-coxalgia, 39.
Psoriasis an infective disorder, 110.
  post vaccinal, 208.
Psycho-analysis and multiple sclerosis, 441.
Psychology and psychotherapy, 245.
  of special senses and their functional disorders, 53.
Psychotherapy, 245.
Pulmonary abscess, 314.
  aspergillosis, 317.
  congestion in typhus, 195.
  lesions, spontaneous and artificial, in guinea-pigs, rabbits, and mice, 154.
  radioscopy and radiography, 581.
Pulmonary streptothricosis, 316.
  suppuration, circumscribed, clinical history of, 581.
  *See also* lung.
Pupil dilatation, paradoxical, following lesions of afferent paths, 550.
Pyelitis larvata cystalgica, 240.
Pyelography in diagnosis of hydatid cysts of kidney, 287.
Pyloric spasm, 6, 184.
Pyrimidine metabolism, 89.

Quartz lamp in treatment of rectal lesions following dysentery, 404.
  ultra-violet therapy and kinetic energy, 391.
Quinine salts, local anaesthesia by, 520.

Radiations, some problems in biological action of, 185.
Radiobiology (abstracts), 93, 185, 395, 487, 585.
Radiodiagnosis (abstracts), 92, 182, 286, 389, 481, 581.
Radiology and electrology (abstracts), 92, 181, 283, 388, 481, 581.
Radiotechnique (abstracts), 181, 290.
Radiotherapy (abstracts), 95, 287, 390, 485, 582.
  deep, in internal medicine, 487.
  prolonged diffuse sclerosis of skin and of cellular tissue of neck following, 391.
Radium, bactericidal action of, on *B. pyocyaneus*, 187.
  emanation, disturbances in development of mammalian embryos caused by, 90.
  —, effect of, on brains of animals, 585.
  —, response of animal organism, to repeated injections of an active deposit of, 185.
  histological changes in bone-marrow of rats exposed to $\gamma$ radiations from, 93.
  Institute, report of work carried out at, during 1919, 96.
  red cell content of those handling, for therapeutic purposes, 93.
  similarity of results produced by vitamines and, 466, 487.
  therapy (abstracts), 96, 283, 392, 583.
Ramus communicans, first white thoracic, in man, 446.
Rat plague, epidemiological and anatomo-pathological observations on, 459.
Rat-bite fever, cases of, 271.
Rays, ultra-violet, visible spectrum, infra-red, phenomena of antagonism between, 395.
Reaction of biological media, 564.
Recto-colitis, severe forms of, 12.
Recurrent laryngeal nerve, paralysis of, 254.
Reflex, pilomotor, 246.
Reflexes, 'conditional', 428.
  labyrinthine, 151.
Regression, numerical law of, of certain sex characters, 179.
Renal complications of influenza, 299.
  function in eclampsia, 539.

Resorcin, intravenous injections of, in treatment of influenza, 305.
Respiration, forced, and tetany, 431.
  physiology of, 382, 383.
Respiratory exchange of surviving mouse tissues, normal and neoplastic, 68.
  diseases, 309.
  infection, acute, microbial studies on, with especial consideration of immunological types, 267.
  quotient and its uncertainty, 383.
  tract, infections of, 267.
Retinitis, albuminuric, 500.
  diabetic, 499.
REVIEWS.
  Active suppuration about the wrist treated by incision dividing the annular ligament, 236.
  Alimentary diseases, 3.
  Anterior dislocation at the elbow, 41.
  Biliary surgery, 125.
  Biochemistry of eclampsia, 537.
  Carotid and vertebral arteries: haemorrhage and aneurysm: cerebral thrombosis and embolism, 322.
  Chancroid, 218.
  Congenital syphilis, 406.
  Congenital torticollis, 132.
  Diabetes mellitus, 497.
  Diphtheria, 18.
  Diseases of the pancreas, 509.
  Diseases of the respiratory system, 309.
  Diseases of the skin, 110.
  Diseases of the spleen, 118.
  Dysentery, 399.
  Electromyogram in nervous diseases, 530.
  Experimental production of alterations in brain volume, 535.
  Gonorrhoea, 210.
  Grafts of dead tendon, 527.
  Influenza, 295.
  Injury causing spasmodic contraction of segments of arteries of medium size, 33.
  Intestinal exclusion, 137.
  Intestinal parasites, 103.
  Melanin, melanoma, melanotic cancer, 229.
  Neurosyphilis, 335.
  Non-tuberculous juvenile coxalgia, 38.
  Physiology of elementary nervous system, 141.
  Physiology of pain, 43.
  Post-mortem examination of a case of arteriovenous aneurysm between the internal carotid artery and the cavernous sinus, 424.
  Rôle of anoxaemia in the production of symptoms in disease and injury of the nervous system, 427.
  Spinal, regional, and local anaesthesia, 516.
  Statistics relating to the treatment of cancer of the breast by excision supplemented by radiation, 418.
  Surgical treatment of chronic intestinal stasis, 221.
  Typhus, 191.
  Vaccination, 205.
  Whooping-cough, 201.
Rickets, aetiology of, 465, 574.
Rickets, dietaries of infants in relation to development of, 176.
  experimental, production of, in rats by deficient diets, 176.
  —, in rats, effect of cod-liver oil on, 176.
Rigor mortis in smooth muscle, 280.
Ringworm, differential diagnosis between large- and small-spored, 112.
  X-ray therapy of, precautions to be taken in, 112.

Sachs-Georgi syphilis reaction, 361.
Sacral anaesthesia, 525.
Saliva in diabetic patients, 499.
Salvarsan, sources of error in treatment by, 158.
  in treatment of pulmonary gangrene, 316.
Saphenous vein, internal, primary sarcoma of, 345.
Saponin, effects of, on respiration, 383.
Sarcoid of Boeck-Darier treated by intravenous injection of salvarsan, 114.
Sarcoma following radium treatment of epithelioma of tongue, 583.
  primary, of internal saphenous vein, 345.
  primary, of stomach, 9.
  of spleen, 120.
Sarcomata of Eustachian tube, 242.
Scabies, 113.
Schmitz, bacteriology of bacillus of, 78.
Sciatica, pathogenesis of, 254.
Sclerodermia, affections of joints in, 113.
Scurvy, protection against, 386, 387.
Secretin, supposed identity of, with water-soluble B vitamine, 468.
Senses, special, psychology of, 53.
Sepsis, chronic, of skin, treatment of, 111.
Septicaemia, gonococcal, 210.
Sera, concentrated, action of, 166.
Serum treatment of chancroid, 220.
  treatment of gonorrhoea, 216.
Sham feeding test, 4.
Shick test for susceptibility to diphtheria, 25.
Shock, experimental, basal metabolism in: oxygen content and chemical changes in blood in, 275.
  lactic acid in blood in, 376.
Silver nitrate solution, use of, for painting throat in treatment of pertussis, 203.
  oligodynamic action of, 480.
  salvarsan in treatment of congenital syphilis, 416.
Skin, diseases of, 110.
  in influenza, 300.
  pigmentation of, 111.
  sensibility to pain of, 45.
Skull, pathological physiology of, 428.
Smell, theory of, 281.
Sodium bicarbonate, relationship between plasma bicarbonate and urinary acidity following the administration of, 173.
  —, solution, intraperitoneal administration of, 480.
  iodide, intravenous injections of, in treatment of gonorrhoeal arthritis, epididymitis, and prostatitis, 214.
  lactate in treatment of diabetes, 506.
Soil bacteria, the size of spores of, 159.

Soil bacteria, a new anaerobic bacillus of (*B. spermoides*), 160.
Soy bean flour, nutritive value of, as a supplement to wheat flour, 468.
Spasmodic contraction of arteries of medium size caused by injury, 33.
Spastic gait, treatment of, by permanent flexion of great toe, 548.
  paralysis, condition of extensor muscles in, 533.
Spectrum, antagonistic properties in different regions of, 396.
Spermatozoa, physical and chemical properties of horse semen in relation to physiology of, 477.
Spinal anaesthesia, 520.
  cord, posterior column of, myelinization of, 547.
  ganglion-cell, human, growth-curve of, 371.
  reflex mechanism, effects of anoxaemia on, 428.
Spine, cervical, congenital anomalies of, 342.
  myeloma of, 250.
Spirillolysis by chorionic ferments, 407.
*Spirochaeta icterohaemorrhagiae*, *Sp. icterogenes*, and *Sp. hebdomadis*, relations of, 455.
Spirochaetes, buccal, beneficial effect of certain bacteria in cultivation of, 270.
  in lymphatic glands, 58.
Spirochaetosis, bronchial, 313.
  ictero-haemorrhagica, dual histopathological character of, relation with acute yellow atrophy of liver, 374.
  spontaneous, of rabbit, 569.
Spironemata of pointed condylomata, 158.
Splanchnic anaesthesia, 524.
Spleen, abscess of, 119.
  diseases of, 118.
  size of, in abdominal cancer, 120.
Splenectomy, indications for, 124.
Splenomegaly, various forms of, 121.
Spores, heat resistance of, 352.
'Staphar' in treatment of chronic sepsis of skin, 111.
Staphylococci, activity of, in milk, 256.
Steatorrhoea, congenital, 509.
*Stegomyia*, period during which, can live at low temperatures, 477.
Stomach, cancer of, 7.
  perforation of, in gastric cancer, 8.
  primary sarcoma of, 9.
  ulcer of smaller curvature of, 182.
  *see also* gastric.
Streptococci, faecal, properties and relations of, 257.
  green producing, respiratory infections with, 267.
  haemolytic, of vermiform appendix, 257.
  haemotoxin of, biological and physical properties of, 69.
  virulence of, action of certain salts on, 361.
Streptococcus empyema, experimental. II. Attempts at dye therapy, 69.
*Streptococcus haemolyticus*, biochemistry of, 565.
  infection, effect of, on reaction of blood of rabbits, 69.
Streptothricosis, pulmonary, 316.
String test in diagnosis of peptic ulcers, 6.
Suggestion, 244.
Sulphur, purgative action of, 180.
Suprarenin solution, immediate death from injection of, 518.
Surgery (abstracts), 52, 239, 341, 435.
Swine erysipelas in man, bacteriology of, 352.
Syphilis, antenatal, 406.
  behaviour of cerebrospinal fluid in, 336.
  congenital, 406.
  —, change of type in, 410.
  —, diagnosis of, 412.
  —, symptomatology of, 410.
  —, treatment of, 414.
  of eighth nerve, 447.
  experimental, superinfection in, following the administration of subcurative doses of arsphenamine or neoarsphenamine, 570.
  and influenza, 302.
  of nervous system, 59, 60, 61.
  of pancreas, 511.
  results of antenatal treatment of, 413.
  Sachs-Georgi reaction in, 361.
  transmission of, to third generation, 412.
  value of gland puncture in early diagnosis of, 59.
  visceral, mistaken for duodenal ulcer, 6.
Syphilitic infection, attenuation of virulence of, in pregnant women, 407.
  aortitis, gastro-intestinal haemorrhage in, 11.

Tabes, behaviour of cerebrospinal fluid in, 337.
  essential lesion of, 547.
  histopathology of, 547.
  juvenile, 149, 411.
  mesenterica following influenza, 302.
*Taenia cucumerina* in infants, 103.
Tar cancer, 114.
Tarsal scaphoid, inflammation of, in young children (Köhler's disease), 483.
Temperature changes induced by gum acacia injections in normal and fevered animals, 90.
Tendon, dead, grafts of, 527.
  reflexes, function of, 531.
Testicle, changes in interstitial tissue of, in consequence of deficiency of water-soluble accessory substance B, 168.
Tetanus toxin, effects of, on artificially perfused liver, 388.
Tetany and forced respiration, 431.
Thiodiglycol, poisonous effect of, upon urease, 179.
Thrombopenia, splenogenous, 124.
Thrombosis, cerebral, 322.
Thrush fungus, 262.
Thyroid apparatus, 475.
  effect of small amounts of, on size and weight of certain organs in male white rat, 280.
  gland, distribution of iodine between cells and colloid in, 475.
  and iodide feeding, comparative effects of, on growth in white rats and rabbits, 179.
  lesions of, in Graves's disease, 247.
Tobacco smoke as disinfectant of mouth, 357.

Tonic fits, 55.
Tonsil, relation of, to blood-vessels, 321.
Tonsils, methods of removing, 326.
Torticollis, congenital, 132.
Trachoma, experimental, 462.
Trauma and diabetes, 497.
Trichocephaliasis, 107, 108.
Trichophytic infection, production of antibodies in, 112.
Trichophytosis complicating vaccination, 208.
Tryptophane, colorimetric experiments on, 579.
Tubercle bacilli, attenuated, antigenic action of, 261.
  comparative value of methods of Herman and Ziehl-Neelsen for staining, 83.
  fat content of, 559.
  human and bovine, facultative acid fastness in, 260.
  search for, in cold abscesses, suppurative glands, and urines, 559.
Tubercle bacillus, cultivation of, in glycerine-free media, 261.
  influence of chaulmoogra oil on, 262.
Tuberculin hypersensitiveness in non-tuberculous guinea-pigs induced by injections of bacillus-free filtrates, 558.
  use of, in lupus erythematosus, 112.
Tuberculosis, active, diagnosis of, by Wildbolz's auto-urine reaction, 559.
  articular, surgical treatment of, 438.
  in bones and joints, radiological diagnosis of, 481.
  of calcaneus in children, 482.
  cutis vegetans, 112.
  and diabetes, 500.
  endothelial reactions in, 375.
  experimental, effect of mustard gas on, 369.
  —, mercury compounds in chemotherapy of, in guinea-pigs, 262.
  influence of exposure to X-rays on the growth of, 395.
  and influenza, 301.
  osseous, surgical treatment of, 438.
  pulmonary, blood ferment in, 162.
  —, suspension stability of blood in, 366.
  of spleen, 120.
  spontaneous, in frog, 84.
  surgical, 435.
  —, actinotherapy of, 437.
Tuberculous sputa, homogenization of, 559.
  guinea-pigs, weight curves of, 82.
Tumours of basal ganglia, mental disturbances in, 447.
  of hypophysis, radiotherapy of, 582.
  malignant, clinically obscure, of nasopharyngeal wall, 242.
  mixed, of facial region, development of so-called, 467.
  of scalp containing brain tissue, 114.
  superficial of brain, 446.
Typhoid fever patients treated with a heterologous (anticholera) vaccine, haematological and serological investigations on, 356.
Typhus, 191.
  in association with other diseases, 196.
  aural and laryngeal complications of, 196.
Typhus, behaviour of body temperature in, in man and in animals that can be experimentally infected, 455.
  blood in, 196.
  bulbo-pontine syndrome in, 195.
  cerebrospinal fluid in, 195.
  diagnosis of, 197.
  epidemiology of, 191.
  incubation period in, 194.
  prophylaxis of, 197.
  pulmonary congestion in, 195.
  relapse in, 194.
  serological studies on, 163, 170.
  symptomatology of, 194.
  treatment of, 198.
  without eruption, 194.
Tyrosinase, 230.

Ulcer, duodenal, treatment of, 14.
Ulcers, gastric and duodenal, 4.
Ulcus molle, 218.
Ultra-violet rays, use of, in preparation of vaccines, 356.
Urea, distribution of, in organism, 576.
Urinary acidity, relationship between, and plasma bicarbonate following administration of sodium bicarbonate, 173.
Urine, estimation of phenolic substances in, 86.
  normal human, experiments on source of variations in reaction of, 385.
  normal and pathological, proteoclastic enzymes in, 385.
  secretion, influence of acacia-glucose injections on, 277.
Urochromogen, 282.
Urticaria, 113.
Uterine fibroids, radium therapy for, 285.
Uterus, involution of, following labour, and influence of castration and sucking on process of involution, 474.
  radiotherapy of carcinoma of, at gynaecological clinic at Erlangen, 288.
  radium treatment of sarcomata of, at gynaecological clinic at Erlangen, 286.

Vaccination, 205.
  complications of, 208.
  prophylactic, of 1,536 persons against acute respiratory diseases, 1919-20, 267.
  statistics, 205.
  technique of, 207.
Vaccine treatment of dysentery, 404.
  treatment of typhus, 199.
  treatment of whooping-cough, 203.
Vaccines, use of ultra-violet rays in preparation of, 356.
Vaccinia, generalized, in Burmese children, 208.
Vagotonia in asthma, 312.
Vagus, irritation of, causing haemorrhagic erosions of stomach, 5.
Vasomotor reactions, peripheral and pulmonary, parallelism between, 167.
Vegetables, sun-dried, antiscorbutic and anti-beri-beri properties of certain, 574.
Veins, functional activity of, 278.

Ventriculography, localization or elimination of cerebral tumours by, 182.
Vertebral artery, 322.
  —, aneurysm of, 330.
  —, ligation of, 330.
  bodies, disappearance of, 372.
  column, rare malformation of cephalic end of, 370.
*Vibrio cholerae*, serological races of, and relation to some other vibrios, 455.
Vitamine content of milk, 84.
  fat-soluble, critique of experiments with diets free from, 177.
  —, differentiation of yellow plant pigments from, 84.
  —, effects of heat, aeration, and ozone on, 84, 85.
  water-soluble B, changes in interstitial tissue of testicle in consequence of deficiency in, 168.
  —, and secretin, supposed identity of, 468.
Vitamines, antiscorbutic and anti-beri-beri in certain sun-dried vegetables, 574.
  distribution of, 468.
  influence of diet of cow upon nutritive and antiscorbutic properties of cow's milk, 177.
  in nutrition of bacteria, 387.
  similarity of effects produced by absence of, and by exposure to X-rays and radium, 466, 487.
Vitiligo, effects of light baths on, 111.
Volatile substances, immediate action of, 477.
Volvulus of sigmoid flexure, surgical treatment of, 227.
Vulva, melanotic cancer of, 234.
Vulvo-vaginitis, gonorrhoeal, in children, treatment of, 217.

Wassermann reaction in chronic splenomegaly, 121.
  in diagnosis of congenital syphilis, 412.
Wassermann reaction in patients affected with malaria in tropics, 357.
  relation of Sachs-Georgi reaction to, 362.
  value of, in pregnancy, 409.
  value of simultaneous testing for, with two different antigens and 'ice-box method', 58.
Water content of human organism, regulation of, 476.
Weil-Felix reaction in typhus, 197.
Wertheim's hysterectomy for advanced carcinoma of cervix made possible by use of radium, 584.
Whitefish sperm, chemistry of, 89.
Wildbolz's auto-urine test for active tuberculosis, 66, 559.
Whooping-cough, 201.
  aetiology of, 201.
  association of, with influenza, 201.
  epidemiology of, 201.
  investigations at State Serum Institute in Copenhagen, 561.
  symptomatology of, 201.
  treatment of, 202.
Wound diphtheria, 23.
  bacteriology of, 162.
Wrist, treatment of acute suppuration of, 236.

X-ray dosage, suggested new method of measuring, 182.
  epitheliomata, treatment of, with radium, 114.
  therapy with new apparatus giving 200,000 volts, 287.
X-rays, similarity of effects produced by vitamines and, 466, 487.
  in treatment of oriental sore, 114.
Xylose, fermentation of, by bacteria of aerogenes, paratyphoid B, and typhoid groups, 77.

Yeast, nutritive value of, in bread, 468.

# II. INDEX OF AUTHORS

Aaser, E., heart failure in diphtheria, 23.
Aaser, P., non-specific horse serum in treatment of diphtheria, 29.
Abderhalden, E., rate of sedimentation of red cells during pregnancy, 543.
  rate of deposition of erythrocytes in plasma and its relation to protective ferments, 175.
Abelin, J., influence of specific iodine compounds upon metamorphosis of frog's larvae and of axolotl, 578.
Abrahamsen, A., Köhler's disease, with special reference to its aetiology, 345.
Abrami, P. : *see* Widal, P., Abrami, P., et Iancoresco, N.
Adams, F. D., carcinoma of pancreas, 513.
Adams, J., antenatal treatment of syphilis, 413.
Adamson, H. G., treatment of lupus vulgaris with liquid acid nitrate of mercury, 112.
  keratodermia blennorrhagica a form of psoriasis, 110, 212.
Adler, F. H., carcinoma of pancreas, 513.
Adolph, E. F., regulation of water content of human organism, 476.
Adrian, C., et Roederer, J., affections of joints in sclerodermia, 113.
Agar, M., treatment of hay fever, 310.
Agnew, F. F., haemorrhage following removal of tonsils, 326.
Agulhon et de Léobardy, J., employment in haematology of complex stains based on Romanowsky principle, 364.
De Albertis, D., quick process for staining neuroglia fibres, 168.
Albu, A., congenital predisposition to peptic ulcer, 5.
  prognosis of dysentery, 403.
  ulcerative colitis a sequel to bacillary dysentery, 401.
Alexandor, H., Wildbolz's auto-urine reaction in diagnosis of active tuberculosis, 559.
Alexander, H. L., precipitin response in blood of rabbits following subarachnoid injections of horse serum, 569.
Alexander, M. E., and Macdonald, E. L., immunity against influenza, 304.
Alexander, W., ligation of vertebral artery, 330.
  inquiry into distribution of blood groups in patients suffering from 'malignant disease', 461.
Alezais et Peyron, development of so-called mixed tumours and cylindromata of facial region, 467.
Alilaire, E., et Fernbach, E., cultivation of tubercle bacillus in glycerine-free media, 261.
Allen, F. M., dietetic treatment of diabetes, 505.
  experimental studies in diabetes. Influence of cold, 276.
  influence of extremes of age, 276.
  influence of fever and intoxication, 275.
  influence of pregnancy upon experimental diabetes, 281.
Allen, F. M., Mitchell, J. W., and Sherrill, J. W., dietetic treatment of diabetes, 506.
Allen, F. M., and Wishart, M. B., exercise in treatment of diabetes, 504.
Alsberg, J., neosalvarsan in treatment of pulmonary gangrene, 316.
Amoss, H. L., immunological distinctions of encephalitis and poliomyelitis, 263.
Amoss, H. L., Gates, F. L., and Olitsky, P. K., simplified production of antimeningococcic serum, 81.
Amsden, H. H., haemorrhage following removal of tonsils, 326.
Andérodias et Dubreuil, G., diabetes and glycosuria, 501.
Anderson, J. F., improved method for production of antimeningococcic and other serums, 82.
Anderson, R. A., and Schultz, O. T., immunologic study of strains of *Bacillus pfeifferi* isolated from a case of meningitis, 561.
André-Thomas, pilomotor reflex, 246.
van Anrep, G., and Drummond, J. C., note on supposed identity of water-soluble vitamine B and secretin, 468.
Antoine, E., severe forms of recto-colitis, 12.
Aoki, K., u. Iizuka, N., studies on subgroups of *Proteus*. Cross-agglutination as differential-diagnostic means, 272.
Apert, E., et Cambessédès, predominance of whooping-cough among females, 201.
Apolloni, G., pancreatic calculi, 514.
Armand-Delille, P. F., intra-muscular route for injection of diphtheria antitoxin, 28.
  prophylaxis of typhus in armies on active service, 197.
Armand-Delille, P. F., et Marie, P. L., Schick test for susceptibility to diphtheria, 26.
Aschenheim, splenic anaemia of infancy, 119.
Ascoli, M., e Fagiuoli, A., treatment of bronchial asthma by irradiation of hypophysis, 312.
Asua, F. J., diseases of spleen, 118.

Aszodi, Z., chemical heat regulation of mammals. Artificial hibernating state in mice, 378.
Aub, J. C., Cunningham, T. D., and Wu, H., experimental traumatic shock. I. The basal metabolism. II. Oxygen content of blood. III. Chemical changes in blood, 275.
Audrain, J., intramuscular injection of ether in treatment of whooping-cough, 202.
Audry, C., tumours of scalp containing brain tissue, 114.
Auguste, C.: *see* Legrand et Auguste, C.
Avery, O. T., and Cullen, G. E., studies on enzymes of pneumococcus. I. Proteolytic enzymes. II. Lipolytic enzymes: esterase. III. Carbohydrate-splitting enzymes: invertase, amylase, and inulase, 71.
Avery, O. T.: *see* Thjøtta, T., and Avery, O. T.
Azzi, A., parallelism between peripheral and pulmonary vasomotor reactions, 167.

Bablet, J., bacteriophagic principle of d'Herelle, 74.
Bach, F. W., comparative studies on races of *Proteus*, with special reference to their capability to produce haemotoxin, 272.
Bacharach, A. L.: *see* Jephcott, H., and Bacharach, A. L.
Bacmeister, A., herpes zoster, infection in, 112.
Bagg, H. J., response of animal organism to repeated injections of an active deposit of radium emanation. Intravenous injections in dogs, 185.
  *see* Gudernatsch, J. F., and Bagg, H. J.
Bagg, H. J., Ewing, J., and Quick, D., experimental study of effects of radium emanation on brains of animals, 585.
Bálint, A.: *see* Hamburger, R., u. Bálint, A.
Ballance, C., and Edmunds, W., ligature of the large arteries in continuity, 329.
Barbour, H. G., and Baretz, L. H., temperature changes induced by gum acacia injections in normal and fevered animals, 90.
Barclay, A. E., danger of Coolidge tube for screen work, 394.
Barcroft, J., anoxaemia, 430.
Bardet: *see* Dobreuilh et Bardet.
Baretz, L. H.: *see* Barbour, H. G., and Baretz, L. H.
Barnes, W. H., activity of staphylococci in milk, 256.
Barr, D. P.: *see* Peters, J. P. (Jr.), and Barr, D. P.
  *see* Peters, J. P., Barr, D. P., and Rule, F. D.
Bársony, T., symptoms due to extreme elongation and dilatation of colon, 14.
Baruch, M., toxic complications following injections into spinal theca, 521.
  *see* Küttner, H., u. Baruch, M.
Basch, S., primary sarcoma of stomach, 9.
Bassett-Smith, P. W., influenza epidemics in the navy, 1918–19, 296.
Bastedo, W. A., surgery in treatment of peptic ulcer, 14.
Bau, A., determination of oxalic-acid and oxaluric acid in urine and faeces, 473.
Baudoin, C., suggestion and auto-suggestion, 244.
Baudrimont, A., bilateral hygroma of pre patellar bursa after influenza, 301.
Baudru, L.: *see* Nanta, A., et Baudru, L.
Bauer, E. L., Shick test for susceptibility to diphtheria, 25.
Bayliss, W. M., psychical disturbances due to oxygen want, 427.
Bazett, H. C.: *see* Corbett, C. D. H., and Bazett, H. C.
Becher, H., oil of turpentine in olive oil in treatment of septic conditions of skin, 111.
Bechhold, W., structure of red blood corpuscles and haemolysis, 367.
Becker, G., complement fixation by hosts of *Bothriocephalus*, 163.
Beckmann, K., haemolytic jaundice, 122.
Beckwith, T. D., and Lyon, R. H., viability and growth of *B. typhosus* in bile, 79.
Béclère, use of radiotherapy in Basedow's disease, 390.
Béclère, A., radium treatment of sarcomata of uterus at gynaecological clinic at Erlangen, 286.
  radiotherapy of carcinoma of uterus at gynaecological clinic at Erlangen, 288.
Béclère, H.: *see* Duval, P., Roux, et Béclère, H.
Behmer, W., biology and biochemistry of *B. proteus* and attempts at the isolation of pathogenic bacteria from *Proteus*-contaminated material by means of agar plates containing carbolic acid or Eichloff-blue, 80.
Behrend, M., improved technique for removal of gall-bladder, 129.
Bell, H. H., relation of different strains of influenza bacilli as shown by cross-agglutination and absorption tests, 155.
Bellot, A.: *see* Degrais, P., et Bellot, A.
Benedetti, U., annular pancreas, 509.
Bennett, T. I., and Dodds, E. C., gastric and respiratory response to meals, 466.
Bensaude, R., et Vicente, M., bile enemata in treatment of constipation, 15.
Bergé, A., et Hufnagel, L., skin eruptions in influenza, 300.
Bergeim, O.: *see* Hawk, P. B., Smith, C. A., and Bergeim, O.
Bergonié, J., heat dermatitis following a chronic X-ray dermatitis, 391.
Berthier: *see* Olmer, D., et Berthier.
Bertolotti, M., congenital anomalies of cervical spine, 342.
  *see* Mattirolo, G., e Bertolotti, M.
Bertoye: *see* Mouriquand, G., et Bertoye.
Besson, A., et de Lavergne, on Morgan's bacillus, 271.
Bettmann, seasonal variations in skin diseases, 111.
Beuttner, O., et Chapuis, R., radium therapy of cancer of cervix, 392.
Bezançon, F., et de Jong, S. I., eosinophilia in sputum in asthma, 311.

Biberfeld, J., acclimatization to drugs. Acclimatization to codein derivatives (eucodal and paracodein), 180.

Bieber, W., diphtheria prophylaxis, 26.
  practical protective value of Behring's toxin-antitoxin mixture against diphtheria, 454.

Bier, A., and Others, 45th conference of German Surgical Society (Surgical Tuberculosis), 435.

Biffis, P., familial haemolytic jaundice, 123.

Bigger, J. W.: *see* Stokes, A., and Bigger, J. W.

Bihlmeyer, G., rashes in diabetic children, 500.

Binet, L.: *see* Rathery, F., et Binet, L.

Bingel, non-specific horse serum in treatment of diphtheria, 28.

Birk, W., non-specific horse serum in treatment of diphtheria, 28.

Birley, J. L., effects of flying at high altitudes, 428.

Bishop, W. A.: *see* Brosius, O. T., and Bishop, W. A.

Bittorf, A., influenza complicated by symptoms of Ménières disease, 301.

Blake, F. G.: *see* Cecil, R. L., and Blake, F. G.

Blake, F. G., and Cecil, R. L., experimental pneumonia. IX. Production in monkeys of an acute respiratory disease resembling influenza by inoculation with *Bacillus influenzae*, 152.

Blake, F. G., and Trask, J. D., susceptibility of monkeys to virus of measles: their symptomatology and pathology when experimentally infected, 354.

Blanc, G., researches on the virus of herpes, 451.

Blanc, J., et Pozerski, E., reaction of biological media, 564.

Blanc, N. E.: *see* Cooper, G. M., Mishulow, L., and Blanc, N. E.

Blanchard, development of phagedaena in vaccine pustule, 208.

Blau, A. I., Shick test for susceptibility to diphtheria, 25.

Bloch, Br., u. Löffler, W., cause of skin colour in Addison's disease, 230, 231.

Bloch, C. E., aetiology of infantile diarrhoea, 12.

Bloomfield, A. L., mechanism of bacillus carrier state with special reference to Friedlaender's bacillus, 467.

Bloor, W. R., blood phosphates in lipaemia produced by acute experimental anaemia in rabbits, 174.
  *see* Sundstroem, E. S., and Bloor, W. R.

Blumenthal, F., results of treatment of cancer of breast by excision and radiation, 420.

Blumenthal, G., aetiology of bacillary dysentery, 272.

Boas, E. P.: *see* Fishberg, M., and Boas, E. P.

Boas, I., cause of gastric ulcer, 5.

de Boer, S., fibrillation of heart, 472.

Bogendörfer, L., effect of sweating and diuretics on blood and body-weight with diet rich and poor in salt, 575.

Böhm, A., epidemiology of influenza, 295.

Boidin, L., diphtheria with multiple and subintrant relapses, 23.

Bolaffi, A., dual histopathological character of spirochaetosis ictero-haemorrhagica: relation with acute yellow atrophy of liver, 374.

Bond, C. J., auto-haemagglutination, 358.

Bonnet, E., et Sicard, J., meaning of term 'emerods' used in Bible, 399.

Bonnet, L. M, et Morenas, large doses of cacodylate of soda in treatment of lichen, 111.

Borchardt, L., u. Ladwig, B, intramuscular injections of milk in influenza, 305.

Bordet, F.: *see* Rathery, F., et Bordet, F.

Bordet, J., theories of blood coagulation, 550.

Bordet, J., et Ciuca, M., leucocytic exudates and transmissible bacterial autolysin, 62.
  production and interpretation of d'Herelle's bacteriophage, 62.

Borelli, E., superficial inguinal hernia, 241.

Boring, E. G., results of experimental nerve section in man, 46.

Bornstein, A., adrenalin glycaemia, 576.

Bornstein: *see* Sänger u. Bornstein.

Bory, M. L., aetiology of psoriasis, 110.

Boss, W., results of treatment of cancer of breast by excision and radiation, 423.

Boughton, T. H., anaphylactic deaths in asthmatics, 311.

Bourges, H., haemolytic jaundice caused by *Ascaris lumbricoides*, 105.

Bourn, J. M.: *see* Stillman, E. G., and Bourn, J. M.

Bradford, J. R., obscure disease of spleen, 121.

Bradley, H. C., and Felsher, H., studies of autolysis. VI. Effect of certain colloids upon autolysis, 86.

Branham, S. E., and Hall, I. C., attempts to cultivate filtrable viruses from cases of influenza and common colds, 264.

Brattström, E., results of treatment of cancer of breast by excision and radiation, 423.

Du Bray, E. S., gastric polyposis, 9.

Du Bray, E. S., and Rosson, F. B., new growths of pleura, 319.

Breinl, F., paragglutination, 355.

Brewster, G. W. W., right colectomy, 224.

Bridge, N., pulmonary streptothricosis, 317.

Briggs, H., physical exertion, fitness, and breathing, 280.

Brigham, F. G., mortality from diabetes, 498; obesity and diabetes, 503.

Brooks, M. M., effects of bile salts and saponin on respiration, 383.

Brosius, O. T., and Bishop, W. A., ankylostomiasis in natives of Zaragosa, 107.

Brown, E. J., local anaesthesia by quinine salts, 520.

Brown, W., psychology and psychotherapy, 245.

Brown, W. H., and Pearce, L., superinfection in experimental syphilis following the administration of subcurative doses of arsphenamine or neoarsphenamine, 570.

Browning, C. H., and Gulbransen, R., antiseptic potency of acriflavine, with considerations on variability of results in testing antiseptics, 465.

Browning, C. H., and Wilson, G. H., antigenic properties of globin, with a note on the independence of properties of serum and tissue proteins as exemplified by absence of antibody from globin of an immunized animal, 165.

Brownlie, J. L., vaccine treatment of diphtheria, 30.

Brun, R., origin and symptomatology of lumbago, 349.

Brüning, H., gastric analysis in children, 3.

Brunn, F., Hitzenberger, K., u. Saxl, P., periodicity of gastric ulcer, 6.

Bruusgaard, E., neurosyphilis, 60.

Bumke, O., troubles due to lumbar puncture, 520.

Bunting, C. H., and Huston, J., fate of the lymphocyte, 572.

Burns, A., relation of tonsil to adjacent arteries, 325.

Burridge, W., researches on perfused heart, 280.

Burrows, A., report of Manchester and District Radium Institute, 283.

*see* Shaw, W. F., and Burrows, A.

Busacca, A., growth-curve of human spinal ganglion-cell, 371.

Bussy, L.: *see* Japiot, P., et Bussy, L.

Butler, E. F., hypertrophic pulmonary osteoarthropathy following lung abscess, 315.

Buttenwieser, S., haemorrhagic encephalitis as complication of dysentery, 402.

Byrne, J., paradoxical pupil dilatation following lesions of afferent paths, 550.

Caius, J. F., and Mhaskar, K. S., chemical composition and therapeutic value of anthelmintics, 106.

Caldarola, P., serological investigations on meningococci, parameningococci, and gonococci, 450.

Calderone, A., experimental investigation on phagocytosis. Influence of diluted solutions of hydrochloric acid, 171.

Calvé, J., non-tuberculous juvenile coxalgia, 39.

Cambessédès: *see* Apert, E., et Cambessédès.

Cameron, A. T., and Carmichael, J., biochemistry of iodine. III. comparative effects of thyroid and iodide feeding on growth in white rats and in rabbits, 179.

Campo, G., modern methods of diagnosis of cancer of stomach, 92.

Cantacuzène, J., Roumanian epidemic of typhus in 1917–18, 191, 195.

Canuyt, G., ulceration of larynx after influenza, 301.

Capelle, anaesthesia of brachial plexus, 525.

Capone, G., studies on anaerobic flora of some morbid states of intestine, 159.

Carini, A., bronchial spirochaetosis, 313.

Carisi, G., primary sarcoma of lung, 318.

Carmichael, J.: *see* Cameron, A. T., and Carmichael, J.

Carnot, P., plastic linitis, 4.

Cartesegna, M., e Casassa, A., diphtheria bacilli in urine of cases, 19.

Carulla, J. E.: *see* Udaondo, C. B., y Carulla J. E.

Casassa, A.: *see* Cartesegna, M., e Casassa, A.

Cassirer, R., u. Lewy, F. H., two cases of superficial brain tumour, 446.

Castigliola, O., treatment of amoebic abscess of liver, 401.

Castronuovo, G., infectious diseases and diabetes, 497.

Cathala, J.: *see* Lian, C., et Cathala, J.

Catsaras, J., fatty embolism in lungs in cases dying of influenza, 298.

Cattoretti, F., haematological and serological investigations on typhoid fever patients treated with heterologous (anticholera) vaccine, 356.

Cauchoix, A., pulsating exophthalmos treated by ligature of both common carotids, 426.

Cazeneuve, H. J., blood in typhus, 196.

Cecil, R. L.: *see* Blake, F. G., and Cecil, R. L.

Cecil, R. L., and Blake, F. G., studies on experimental pneumonia. X. Pathology of experimental influenza and of *Bacillus influenzae* pneumonia in monkeys, 153.

Cecil, R. L., and Steffen, G. I., acute respiratory infection in man following inoculation with virulent *B. influenzae*, 264.

Celsus, old methods of removal of tonsils, 326.

Cernezzi, A., treatment of large umbilical and ventral hernias, 239.

Chapuis, R.: *see* Beuttner, O., et Chapuis, R.

Chaput, treatment of acute suppuration of wrist, 236.

Chartier, treatment of medullary and radical after-effects of epidemic encephalomyelitis, 493.

Chatellier, L., erythromelalgia cured by single injection of adrenalin, 113.

Chaton et Sauvé, grafts of dead tendon, 529.

Chauffard, immunity against influenza, 304.

Chauveau, A., absence of internal carotids in sheep, 323.

Cheinisse, treatment of chancroid, 219.

Cheinisse, L., intramuscular injection of ether in treatment of whooping-cough, 202.

prophylaxis of influenza, 305.

Cheplin, H. A., and Rettger, L. F., intestinal implantation of *Bacillus acidophilus*, 90, 178.

Chesney, A. M.: *see* Rowntree, L., Chesney, A. M., and Marshall E. K.

Chevrotier, J.: *see* Lumière, A., et Chevrotier, J.

Chicandard, M., tuberculosis of calcaneus in children, 482.

Chievitz, O., Jenson, J., Reyn, A., and Collin, E., surgical treatment of osseous and articular tuberculosis, 438.

Chiray, M., excretion of glycuronates in cases of vomiting of pregnancy, 541.

Chotzen, T.: *see* Schaeffer, F., and Chotzen, T.

Christiansen, M., gas phlegmon following subcutaneous injections, 568.

Christensen, S.: *see* Thomsen, O., and Christensen, S.

Churchman, J. W., cause of parallelism between Gram reaction and gentian violet reaction. Isolation of gentian-positive individuals from a suspension of a gentian-negative organism. Relation of gentian violet reaction to dilution of implanted suspension. Effect of repeated re-inoculations of gentian violet agar with gentian-positive organisms. Selective action of gentian violet in relation to chemotherapy. Communal activity of bacteria, 91.

Ciani, G., cultures of anaerobic germs in ordinary Petri dishes in presence of air, 354.

Ciccarelli, F., transient polyomyelitis after influenzal broncho-pneumonia, 299.

Cinca, M.: *see* Bordet, J., et Cinca, M.

Civatte, A., et Vigne, P., treatment of sarcoid of Boeck-Darier by intravenous injection of salvarsan, 114.

Clément, R.: *see* Ramond, F., et Clément, R.

Clemow, F. G., typhus in Turkey, 193.

Clendening, L., pulmonary abscess, 315.

Cluzet, Rochaix, et Kofman, bactericidal action of radium on *B. pyocyaneus*, 187.

Coca, A. F., and Kelley, M. F., serological study of bacillus of Pfeiffer, 267.

Cockcroft, W. L., Loewi's adrenalin test for pancreatic insufficiency, 514.

Cohen, C., on formation of acetaldehyde during decomposition of sugar by moulds, 388.

Cohen, M., and Levin, I., action of radium in cataract, 285.

Cole, L. G., and Roberts, D., duodenal diverticula: their clinical and radiological aspect, 183.

Collignon: *see* Monziols et Collignon.

Collin, E.: *see* Chievitz, O., Jensen, J., Reyn, A., and Collin, E.

Collip, J. B., effect of surgical anaesthesia on reaction of blood, 67.

Connell, A. A., Cyst of common bile-duct, 128.

Conseil, E.: *see* Nicolle, C., et Conseil, E.'

Constantinesco, C. D., et Sloboziano, typhus without eruption, 194.

Cooke, J. V., complement fixation in influenza with *B. influenzae* antigens, 155.

Cooper, G.: *see* Park, W. H., and Cooper, G.

Cooper, G. M., Mishulow, L., and Blanc, N. E., study of the serological relationships of pneumococci from the upper respiratory tract, with special reference to common colds and influenzal conditions, 267.

Corbett, C. D. H., and Bazett, H. C., cerebral effects of oxygen want, 431.

Corinaldesi, S., jaundice in influenza, 299.

Corper, H. J.: *see* Hektoen, L., and Corper, H. J.

Corper, H. J., and Rensch, O. B., effect of mustard gas on experimental tuberculosis, 369.

La Coste et Ferrier, injury causing spasmodic contraction of arteries, 33.

Costiniu, A., aural and laryngeal complications of typhus, 196.

Cottin, E., Cramer, A., et Saloz, C., cancer of lung, 317.

Couillaud, F., tongue sign in helminthiasis, 103.

Coulet, G., fatal tonsillar abscess after influenza, 301.

Coulter, C. B., equilibrium between haemolytic sensitizer and red blood cells in relation to hydrogen-ion concentration, 378.
  isoelectric point of red blood cells and its relation to agglutination, 176.

Courcoux: *see* Legry, Courcoux, et Lermoyez, J.

Coutela, C., retinitis in diabetics, 500.

Cowan, M. L.: *see* Maitland, H. B., Cowan, M. L., and Detweiler, H. K.

Coward, K. H.: *see* Drummond, J. C., and Coward, K. H.
  *see* Drummond, J. C., Golding, J., Zilva, S. S., and Coward, K. H.

Cramer, A.: *see* Cottin, E., Cramer, A., et Saloz, C.

Cramer, W., and Mottram, J. C., similarity of effects produced by absence of vitamines and by exposure to X-rays and radium, 466, 487.

Cranston Low, R., Logan, W. R., and Rutherford, A., fatal case of lupus erythematosus, 112.

Cristol et Porte, gas cysts of abdomen, 11.

Crohn, B. B., and Reiss, J., effects of restricted (so-called ulcer) diets upon gastric secretion and motility, 15.

Cron, R. S., glycosuria and pregnancy, 501.

Crouter, C. Y.: *see* Hendrix, B. M., and Crouter, C. Y.

Crowell, B. C., distribution and effects of *Ascaris lumbricoides*, 104.

Cuénod, A.: *see* Nicolle, C., et Cuénod, A.

Cullen, G. E.: *see* Avery, O. T., and Cullen, G. E.

Cullis, W. C., and Hewer, E. E., 'ammonia coefficient' of pregnancy, 89, 538.

Culver, G. D.: *see* Montgomery, D. W., and Culver, G. D.

Cunningham, T. D.: *see* Aub, J. C., Cunningham, T. D., and Wu, H.

Curatolo, F., sodium lactate in treatment of diabetes, 506.

Curschmann, H., defects of endocrine glands in causation of bronchial asthma, 310.

Cushing, H., and Foley, F. E. B., alteration of intracranial tension by salt solution in alimentary canal, 178.

Cutler, E. C., abscess of spleen following otitis media, 119.

Dahle, C. H.: *see* Dutiker, R. A., Eckles, C. H., Dahle, C. H., Mead, S. W., and Schaefer, O. G.

Daken, J., treatment of gonorrhoeal vulvovaginitis in children, 217.

Dandy, W. E., diagnosis and treatment of hydrocephalus due to occlusion of foramina of Magendie and Luschka, 549.
  localization or elimination of cerebral tumours by ventriculography, 182.

Daniels, A. L., and Loughlin, R., deficiency of heat-treated milks, 85.

Danis, M., inflammation of cellular tissue of right orbit following influenzal pneumonia, 301.

Darier, J., myiasis cured by excision, 114.

Darier, J., precancerous dermatosis, 114.
Darier, J., et Hallé, J., naevus derived from bronchial clefts, 114.
Darling, S. T., mass treatment of hookworm infection, 107.
Daubit, polysulphide of calcium in treatment of scabies, 113.
Davey, A. J., determination of minimum doses of some fresh citrus fruit juices which will protect a guinea-pig from scurvy, together with some observations on preservation of such juices, 386.
Davide, H. L., aetiology of influenza, 563.
Davis, L. C.: see Kolmer, J. A., Davis, L. C., and Jager, R.
Davis, L. H.: see Ross, E. L., and Davis, L. H., 274.
Davis, L. H., and Ellison, L. R., source of diastases in blood, 469.
Davis, T. K.: see Kirby, G. H., and Davis, T. K.
Davison, W., divisions of so-called Flexner group of dysentery bacilli, 77.
Davison, W. C., ileo-colitis in children in Maryland and Alabama due to *B. dysenteriae*, 400.
Dawson, P. R.: see Sullivan, M., and Dawson, P. R.
Deaver, H. C., cholecystitis following typhoid, 127.
Deaver, J. B., McFarland, J., and Herman, J. L., statistics relating to treatment of cancer of breast by excision and radiation, 419.
Debré, R., et Haguenau, some peculiarities of 'd'Herelle phenomenon', 74.
Degrais, P., et Bellot, A., treatment of X-ray epitheliomata with radium, 114.
Deibert, O.: see Teague, O., and Deibert, O.
Delherm et Laquerrière, electro-radiology in neuritis of motor nerves, 492.
Delmas, P., general analgesia by cocaine injected into spinal theca, 522.
Denk, W., general and local anaesthesia, 516.
  intestinal exclusion, 137.
Denny, H. T.: see Povitsky, O. R., and Denny, H. T.
Dercum, F. X., intraspinal treatment of neurosyphilis with salvarsanized serum, 338.
Desderi, P.: see Volpino, G., e Desderi, P.
Dessane: see Gougerot et Dessane.
Detweiler, H. K.: see Maitland, H. B., Cowan, M. L., and Detweiler, H. K.
Deuel, jun., H. J.: see Holmes, A. D., and Deuel, jun., H. J.
Dible, J. H., enterococcus and faecal streptococci: their properties and relations, 257.
Dickson, W. E. C., congenital obliteration of bile-ducts, 127.
Dide et Guiraud, special staining method for lipoid granules in nerve-cells, 252.
Dienst, A., eclampsia due to thrombus formation, 543.
Diez, S., trauma and diabetes, 497.
Di Macco, G., on influence of nutrose in culture medium of Drigalski-Conradi, 77.
  experimental investigations on phagocytosis. Influence of fatigue, 171.
  see Musumeci, G., e Di Macco, G.
Dind, M., lichen and lichenification, 111.
Dixon, W. E., and Ransom, F., immediate action of volatile substances, 477.
Dobreuilh et Bardet, deformities of hands since childhood caused by cicatrices, 482.
Dodds, E. C.: see Bennett, T. I., and Dodds, E. C.
Doerr, R., oligodynamic action of silver, 480.
Doerr, R., Schnabel, A., u. Vöchting, K., behaviour of body temperature in typhus in man and in animals that can be experimentally infected, 455.
Dold, H., und Fischer, W., a case of naturally acquired bacillary dysentery in dog with simultaneous schistosomiasis, ankylostomiasis, and filariasis, 79.
Dopter, C., immunity against influenza, 303.
Doran, A., melanotic cancer of vulva secondary to adrenal tumour of kidney, 234.
Dorland, N., methylene blue in treatment of gonorrhoea in women, 216.
Douglas, S. R., question of serological races of *V. cholerae* and relation of some other vibrios to this species, 455.
Downey, H.: see Mandlebaum, F. S., and Downey, H.
Dragstedt, L. R., effect of *Streptococcus haemolyticus* infection on reaction of blood of rabbits, 69.
Draper, G., acute poliomyelitis, 146.
Dreyer, G., simple procedure for accurate enumeration of blood-cells and bacteria without the use of a counting chamber, 364.
Dreyfus, G. L., constitution of cerebrospinal fluid—deciding factor for prognosis and therapy in syphilis of nervous system, 59, 336.
Drummond, J. C., nutrition on diets practically devoid of fat, 178.
  see van Anrep, G., and Drummond, J. C.
Drummond, J. C., and Coward, K. H., researches on fat-soluble accessory factor (Vitamine A.) VI. Effect of heat and oxygen on nutritive value of butter, 84.
Drummond, J. C., Golding, J., Zilva, S. S., and Coward, K. H., nutritive value of lard, 85.
Drüner, hemiplegia following ligature of common carotid, 324, 328.
Dubourg et Guénard, F., mortality from diphtheria in children's hospital in Bordeaux from 1888 to 1917, 18.
Dubreuil, G.: see Andérodias et Dubreuil, G.
Dubreuilh, W., infective pruriginous eruption among Tonkinese and Annamites, 113.
Ducceschi, V., influence of ethyl alcohol on organism, 463.
Duchemin, B., sarcoma of spleen, 120.
Dudgeon, L. S., blackwater-fever, 457.
Dufour, H., Semelaigne, G., et Ravina, A., pulmonary gangrene cured by antigangrene serum, 316.
Dufourt, A.: see Weill, E., et Dufourt, A.
Dumas, J., on presence of bacteriophage in healthy intestine, in soil, and in water, 74.
Dumitresco-Mante, three forms of pulmonary congestion in typhus, 195.

Duncan, A. G. B.: *see* Fraser, A. R., and Duncan, A. G. B.
Dunham, J. H., visceral syphilis mistaken for duodenal ulcer, 6.
Dupérié, R., treatment of congenital syphilis with subcutaneous injections of novarsenobenzol and novocaine, 416.
Dupuy, test of sham feeding, 4.
Durand, M., grafts of dead tendon, 528.
Duroeux, L.: *see* Lévy-Bing, A., et Duroeux, L.
Dutiker, R. A., Eckles, C. H., Dahle, C. H., Mead, S. W., and Schaefer, O. G., Vitamine studies. VI. Influence of diet of the cow upon nutritive and antiscorbutic properties of cow's milk, 177.
Duval, P., Roux, et Béclère, H., ulcer of smaller curvature of stomach, 182.
Dwyer, H. L., malignant endocarditis due to *Gonococcus*, 211.
van Dyke, H. B., study of distribution of iodine between cells and colloid in thyroid gland. III. Effect of stimulation of vagosympathetic nerve on distribution and concentration of iodine in dog's thyroid gland, 475.

Ebaugh, F. G., and Stevenson, G. S., measurement of intracranial pressure changes in an epileptic, and its experimental variation, 536.
Eberle, D., invasion of pancreas by ascarides, 104.
Eby, H.: *see* Howell, K. M., and Eby, H.
Eckles, C. H.: *see* Dutiker, R. A., Eckles, C. H., Dahle, C. H., Mead, C. W., and Schaefer, O. G.
Edmunds, W.; *see* Ballance, C., and Edmunds, W.
Ege, R., distribution of glucose between plasma and red blood corpuscles. Physiology of blood sugar, 377, 471.
Einhorn, M., duodenal perforation treated by duodenal alimentation, 15.
  string test in diagnosis of peptic ulcers, 6.
  treatment of impermeable cardiospasm, 15.
Eiskamp, E. H., and Park, L. K., fate of micro-organisms introduced into isolated loops of intestine, 79.
Eitner, E., electrolysis treatment of hypertrichosis, 114.
Ellermann, V., new strain of transmissible leukaemia in fowls (strain H), 572.
Ellis, N. R.: *see* Hart, E. B., Steenbock, H., and Ellis, N. R.
Ellison, L. R.: *see* Davis, L. H., and Ellison, L. R.
Emge, L. A., acidosis in pregnancy, 537.
Engelbreth, C., influenza transmitted through fleas, 296.
Erlanger, J., blood-pressure estimation by indirect methods. Movements in artery under compression during blood-pressure determinations, 378.
  *see* White, H. L., and Erlanger, J., 273.
Ernst, N. P., actinotherapy of surgical tuberculosis, 437.
Epstein, J. W., intraperitoneal administration of sodium bicarbonate solution, 480.
Evans, C. L., cyanide anoxaemia, 429.
  on probable error in determinations by means of hydrogen electrode, 255.
Ewing, J.: *see* Bagg, H. J., Ewing, J., and Quick, D.
Ewing, J., and Wolf, C. G. L., ammonia coefficient in eclampsia, 339.
Eyster, J. A. E.: *see* Meek, W. J., and Eyster, J. A. E.

Fagiuoli, A.: *see* Ascoli, M., e Fagiuoli, A.
Fahr, renal lesions in eclampsia, 540.
Failla, G., radium technique at Memorial Hospital, New York, 290,
Fairbank, H. A. T., pseudo-coxalgia—osteochondritis deformans juvenilis, 39.
Falcioni, D., immunity against influenza, 304.
Falta, W., u. Richter-Quittner, M., chemical composition of blood-corpuscles, 579.
Farah, N., bronchial spirochaetosis, 313.
Farnell, F. J., and Harrington, A. H., acute infectious enteritis with a polyneuritic syndrome, 12.
Favrat: *see* Maisonneuve et Favrat.
Feigl, J., appearance and distribution of fats and lipoids in blood after bleeding. Chemical contribution to knowledge of lipaemia, 376.
  composition of liver in acute yellow atrophy, 479.
Felsher, H.: *see* Bradley, H. C., and Felsher, H.
Fenn, W. O., phagocytosis of solid particles. I. Quartz. II. Carbon, 478.
Fernbach, E.: *see* Alilaire, E., et Fernbach, E.
Ferrier: *see* La Coste et Ferrier.
Feucht, B., Bürker's method for blood counts, 277.
Feulgen, R,: *see* Stepp, W., and Feulgen, R.
Ficai, G., serological studies on typhus, 163.
Field, C. G., non-tuberculous lung infection, 313.
Fildes, P., nature of effect of blood-pigment upon growth of *B. influenzae*, 156.
Le Filliatre, G., general analgesia by cocaine injected into spinal theca, 522.
Findlay, L., treatment of congenital syphilis, 414.
Fineman, B. C., study of thrush parasite, 262.
Finks, A. J.: *see* Johns, C. O., and Finks, A. J.
Finochietto, R.: *see* Vaccarezza, R. F., y Finochietto, R.
Finsterer, H., ascites in connexion with duodenal ulcer, 5.
  general and local anaesthesia, 516.
  intestinal exclusion, 138.
Fiolle, J., injury causing spasmodic contraction of arteries, 33, 35.
Fischer, A. W., death from injection of suprarenin solution, 518.
Fischer, W.: *see* Dold, H, u. Fischer, W.
Fishberg, M., and Boas, E. P., outbreak of influenza in tuberculosis pavilion of Montefiore Hospital, New York, 301.

Fisher, A. G. T., absence of internal carotids in a man, 323.

Fitz, R., diabetes and leukaemia, 501.

  surgical complications of diabetes, 500.

Fletcher, H. M., change of type in congenital syphilis, 410.

Flu, P. C., period during which stegomyia can live at low temperatures, 477.

Foges, A., treatment of rectal lesions following dysentery with quartz lamp, 404.

Földes, E., u. Hajós, K., treatment of influenza by subcutaneous injections of normal horse serum, 305.

Foley, F., fall in cerebrospinal fluid pressure produced by injections of hypertonic salt solutions, 536.

Foley, F. E. B.: *see* Cushing, H., and Foley, F. E. B.

Foley, F. E. B., and Putnam, T. J., experimental production of alterations in cerebrospinal fluid pressure and brain volume, 535.

Folin, O., level of blood area in normal pregnancy, 539.

Fontaine, J., measurement of arterial blood-pressure in horses, 279.

Fontana, A., e Sangiorgi, G., on spironemata of pointed condylomata, 158.

Foot, N. C., endothelial reactions in tuberculosis, 375.

Forbes, A., and Rappleye, W. C., rhythm of human electromyogram, 531.

Fordyce, J. A., and Rosen, I., intramuscular injections of neosalvarsan and an oily suspension of mercury in treatment of congenital syphilis, 414.

Forestier, J.: *see* Loeper, M., Forestier, J., et Tonnet, J.

Forestier, J., et Michon, L., pyelography in diagnosis of hydatid cysts of kidney, 287.

Förssell, G., radiological diagnosis of tuberculosis in bones and joints, 481.

Foster, L. F., relation of hydrogen-ion concentration to growth, viability, and fermentative activity of *Streptococcus haemolyticus*, 565.

  biochemistry of *Streptococcus haemolyticus*, 565.

Foster, L. F., and Randall, S. B., study of variations in hydrogen-ion concentration of broth media, 566.

Franz, L., chemotherapeutic experiments with a view to treatment of diphtheria of wounds, 355.

Fraser, A. R., and Duncan, A. G. B., vaccine treatment of diphtheria, 30.

Frassi, L., injury causing spasmodic contraction of arteries, 37.

Fred, E. B., and Peterson, W. H., fermentation of xylose by bacteria of aerogenes, paratyphoid B, and typhoid groups, 77.

Freeman, R. G., vaccine treatment of whooping-cough, 203.

Freudenberg, E., u. György, P., calcium combination with animal tissues, 478.

Freund, J.: *see* Rothfeld, J., Freund, J., u. Hornowski, J.

v. Frey, M., contraction of muscle treated with veratrin, 532.

Frieberg, F., actinotherapy in three cases of tumour of hypophysis, 486.

Friedenwald, J., and Grove, G. H., blood-sugar tolerance in gastro-intestinal carcinoma, 8.

Friedmann, J. C., non-specific intestinal infection, 12.

Fries, J. A., respiratory quotient and its uncertainty, 383.

Fritzsche, R., primary parenchymatous haemorrhage from stomach, 11.

Frohlich, A., u. Meyer, H., electromyogram in tetanus, 533.

Frouin, A., fat content of tubercle bacilli of human, bovine, and avian types respectively, 559.

Frühwald, R., spirochaetes in lymphatic glands, 58.

Fukuda, A., experiments on anthrax in rats, 161.

Fürbringer, prevalence of *Oxyuris vermicularis* caused by war, 105.

Furno, A., chronic lung disease following influenza, 297.

Fürth, on antigenic action of attenuated tubercle bacilli, tortoise and other acid-fast bacilli, 261.

Fürth, O., u. Lieben, F., colorimetric experiments on tryptophane. IV. Formation of melanoidin in acid hydrolysis of proteins and its dependence upon tryptophane complexes. V. Our knowledge of proteins of immune sera and their tryptophane content, 579.

Futcher, T. B., carcinoma of pancreas, 512.

Gad Andresen, K. L., distribution of urea in organism, 576.

Galambos, A., renal glycosuria, 503.

Galdi, F., pulmonary aspergillosis, 317.

Galewsky, E., eczema caused by leather substitute in hat linings, 111.

  'staphar' in treatment of chronic sepsis of skin, 111.

Gallerand: *see* Ravaut, P., et Gallerand.

Gamma, G., special microscopic finding in nervous tissue from cases of lethargic encephalitis, 452.

Gammeltoft, S. A.: *see* Hasselbach, K. A., u. Gammeltoft, S. A.

Gane, T., relapse in typhus, 194.

Gardner, E. L.: *see* Henrici, A. T., and Gardner, E. L.

Garrod, A. E., diagnosis of disease of pancreas, 514.

Gates, F. L.: *see* Amoss, H. L., Gates, F. L., and Olitsky, P. K.

Gates, F. L.: *see* Olitsky, P. K., and Gates, F. L.

Gates, F. L., and Olitsky, P. K., factors influencing anaerobiosis, with special reference to use of fresh tissues, 454.

Gay, D. M.: *see* Putnam, J. J., and Gay, D. M.

Gay, F. P., and Morrison, L. F., experimental streptococcus empyema. II. Attempts at dye therapy, 69.

Gentili, A., secretory activity of anterior lobe of pituitary body during pregnancy, 371.
Genoese, G., cerebrospinal fluid in whooping-cough, 202.
Gerber, I. : *see* Turretini, G., et Gerber, I.
De Géry, C. P., gas cysts of abdomen, 10.
Gessner, W., Baden statistics of eclampsia during the war, 543.
Giese, G. : *see* Kossel, A., u. Giese, G.
Giffin, H. Z., persistent eosinophilia with hyperleucocytosis and splenomegaly, 122.
  tuberculosis of spleen, 120.
Gilliatt, W., and Kennaway, E. L., ammonia coefficient in cases of pernicious vomiting in pregnancy, 538.
Gioseffi, M., skin eruptions in influenza, 300.
Giuliani, R., sexual neutralization obtained by means of orchilytic and ovariolytic sera, 169.
Glaessner, K., gastric and pancreatic secretions in bacillary dysentery, 401.
Glass, E., mixed-celled sarcoma of lung, 318.
Glatard, epidemic of typhus in Algeria, 197.
  treatment of typhus by intravenous injections of urotropin, 198.
Gleyvod, P., intramuscular injection of ether in treatment of whooping-cough, 202.
Golay, M. J., Fontan's method of treating chancroidal buboes, 220.
Goldberg, B., influenzal haematuria, 299.
Goldberg, J. M. : *see* Strickler, A., and Goldberg, J. M.
Goldberger, I. H., use of inner and back sides of arm for vaccination, 207.
Golding, J. : *see* Drummond, J. C., Golding, J., Zilva, S. S., and Coward, K. H.
Goldman, A. : *see* Grant, S. B., and Goldman, A.
  *see* Williams, A. W., Unneberg, A., Goldman, A., and Hussey, H.
Goodall, E. W., typhus in Poland, 1916–19, 191.
Goodall, J. R., vaccination by subcutaneous injection, 207.
Göppert, F., umbilical diphtheria, 22.
Gougerot, complications of vaccination, 208.
Gougerot et Dessane, treatment of warty naevus in heredo-syphilitic subject, 410.
Gourbis, atonic syndrome of digestive tract in nervous persons, 389.
Gracey, G. F., hemiplegia following tonsillectomy, 327.
Graham, G., dysenteric arthritis at Malta, 401.
Graham, S. G.: *see* Imrie, C. G., and Graham, S. G.
Graham Brown, T., scratch reflex in guinea-pigs, 429.
Gram, H. C., volume of red blood corpuscles and ratio of this volume to haemoglobin and to number of cells, 365.
Gramén, K., Wildbolz's auto-urine test for active tuberculosis, 66.
Grant, S. B., and Goldman, A., tetany produced by forced respiration, 432.
Gray, G. A., and Meyer, B. I., diphtheria carriers and their treatment with mercurochrome, 454.
Griffiths, G. H. St. Geo., disadvantages of novocaine as local anaesthetic, 520.
Groebel, W. : *see* Trendelenburg, P., u. Groebel, W.
Groedel, F. M., radiological appearances of encapsuled pleural effusions, 581.
Grönberg, J., blood ferment in pregnancy, carcinoma, and pulmonary tuberculosis, 162.
Gross, A. : *see* Korbsch, R., u. Gross, A.
Gross, O., forms of pancreatitis, 510.
Grossfeld, H., onychodystrophy following typhus, 195.
Groth, A., results of vaccination in Bavaria, 205.
Grothusen, dysenteriform catarrh of large intestine due to flagellata, 399.
Grove, G. H. : *see* Friedenwald, J., and Grove, G. H.
Gudernatsch, J. F., and Bagg, H. J., disturbances in development of mammalian embryos caused by radium emanation, 90.
Guénard, F. : *see* Dubourg et Guénard, F.
Guillain, G., epileptic convulsions in patient with diabetes and acetonuria, 499.
Guimbellot, surgical treatment of volvulus of sigmoid flexure, 227.
Guirard : *see* Dide et Guirard.
Guisez, J., treatment of cancer of oesophagus and of larynx by local applications of radium, 285.
Gulbransen, R. : *see* Browning, C. H., and Gulbransen, R.
Gunn, J. A., and Heathcote, R. St. A., cellular immunity : observations on natural and acquired immunity to cobra venom, 360.
Gurley, C. R. : *see* Williams, A. W., Nevin, M., Gurley, C. R.
György, P., sedimentation of blood corpuscles, 377.
  *see* Freudenberg, E., György, P.

Habermann, R., u. Mauelshagen, F., value of gland puncture in early diagnosis of syphilis, 59.
Haffner, R., relation of placental infarcts and albuminuria, 544.
Haggard, H. W., anaesthetic and convulsant effects of gasoline vapour, 280.
Haggard, H. W., and Henderson, Y., haemato-respiratory functions. IX. An irreversible alteration of $H_2CO_3/NaHCO_3$ equilibrium of blood induced by temporary exposure to a low tension of $CO_2$, 174.
Haggard, W. D., primary sarcoma of stomach, 9.
Haguenau : *see* Debré, R., et Haguenau.
Hahn, M., u. Skramlik, E., experiments with antigens and antibodies upon surviving artificially perfused liver. Tetanus toxin, 388.
Hajós, K. : *see* Földes, E., u. Hajós, K.
Haldane, J. S., Kellas, A. M., and Kennaway, E. L., effects of oxygen want, 431.
Haldane, J. S., and Poulton, E. P., effects of oxygen want, 431.

Hall, I. C., chemical criteria of anaerobiosis with special reference to methylene blue, 453.
*see* Branham, S. E., and Hall, I. C.
Hallé, J. : *see* Darier, J., et Hallé, J.
d'Halluin, M., electric currents which kill. The mode of death. How life may be saved, 587.
Hamburger, R., u. Bálint, A., influenza in children, 303.
Hamburger, W. W., post-influenzal myocardial involvement, 298.
Hammett, F. S., studies of the thyroid apparatus. I. Stability of nervous system as factor in resistance of albino rat to loss of parathyroid secretion, 475.
Handley, S., treatment of cancer of breast by excision combined with radiation, 419.
Hanganut, M., intravenous injections of resorcin in treatment of influenza, 305.
Hansen, O. S., magnesium sulphate in arsenic poisoning, 282.
Harbitz, F., encephalitis neonatorum, 253.
Hári, P., light absorption of reduced haemoglobin, 376.
Harman, B., blindness due to congenital syphilis, 411.
Harrington, A. H. : *see* Farnell, F. J., and Harrington, A. H.
Harry, F., blood in influenza, 296.
Hart, E. B., Steenbock, H., and Ellis, N. R., antiscorbutic potency of milk powders, 468.
Hartwell, G. A., effect of diet on mammary secretion, 387.
Harvier, P. : *see* Levaditi, C., Harvier, P.
Hasselbach, K. A., u. Gammeltoft, S. A., acidosis in normal pregnancy, 537.
Haughwout, F. G., and Lantin, P. T., treatment of dysentery with benzyl benzoate, 404.
Haugseth, K., Dakin's solution in treatment of wound diphtheria, 30.
Hawk, P. B. : *see* Rehfuss, M. E., and Hawk, P. B.
Hawk, P. B., Smith, C. A., and Bergeim, O., nutritive value of yeast in bread, 468.
vitamine content of honey, 468.
Head, H., protopathic sensibility, 142.
Head, H., Rivers, W. H. R., and Sherren, J., results of experimental nerve section in man, 46.
Heathcote, R. St. A. : *see* Gunn, J. A., and Heathcote, R. St. A.
Hedblom, C. A., pulmonary abscess, 314.
Hedenius, J. : *see* Strandberg, J., et Hedenius, J.
Hedin, S. G., proteoclastic enzymes in normal and pathological urines, 385.
Heermann, treatment of hay fever, 310.
Hehewerth, F. H., and Kop, W. A., Wassermann test in patients affected with malaria in the tropics, 357.
Heissen, F., hereditary factor in bronchial asthma, 310.
Heitz, J. : *see* Leriche, R., et Heitz, J.
Hektoen, L., and Corper, H. J., effect of mustard gas on antibody formation, 369.
Helferich, treatment of acute suppuration of wrist, 237.
Heller, H. H., aetiology of acute gangrenous infections of animals: a discussion of blackleg, braxy, malignant oedema, and whale septicaemia, 160.
Henderson, L. J., blood as a physico-chemical system, 469.
*see* McLean, F. C., Murray, H. A., jun., and Henderson, L. J.
Henderson, Y., apnoea after forced respiration, 432.
*see* Haggard, H. W., and Henderson, Y.
Hendricks, H. V., chylous ascites due to carcinoma of stomach, 8.
Hendrix, B. M., and Crouter, C. Y., relation of alkali reserve of blood to glycosuria and hyperglycaemia in pancreatic diabetes, 173.
Hendry, R. A., antenatal syphilis, 406.
Henestenberg, W., acanthosis nigricans with carcinoma of internal organs, 114.
Henkel, M., umbilical diphtheria, 22.
Hennebert, C., deafness due to congenital syphilis, 411.
Henrici, A. T., and Gardner, E. L., acid-fast actinomycetes, with report of case from which a new species was isolated, 261.
Henriksen, P. B., cultivation of nerve-tissue and nerve regeneration, 351.
Heppner, M. : *see* Stevens, W. E., and Heppner, M.
d'Herelle, F., on nature of bacteriophagic principle, 74.
on bacteriophagic microbe, 74.
Hering, F., toxic effects of injection of novocaine and bicarbonate solution into a vein, 519.
Herman, J. L. : *see* Deaver, J. B., McFarland, J., and Herman, J. L.
Hermanies, J., gonococcus types, 257.
Herring, weight of organs in pregnancy, 540.
Hertz, R., value of Wassermann reaction in diagnosis of congenital syphilis, 412.
Herzfeld, E., non-specific horse serum in treatment of diphtheria, 28.
Herzog, F., bothriocephalus anaemia, 108.
Herzog, F., u. Zeller, H., uromelanin and uromelanogen, 229.
Hess, A. F., and Unger, L. J., dietaries of infants in relation to development of rickets, 176.
Hess, R., blood picture in whooping-cough, 202.
Hesse, E., u. M., frequency of gall-stones, 127.
Hesse, W., auscultatory sign for diagnosis of laryngeal diphtheria, 24.
Hewer, E. E. : *see* Cullis, W. C., and Hewer, E. E.
Hewer, R. : *see* Cullis, W. C., and Hewer, R.
Hewitt, J. A., effect of administration of small amounts of thyroid gland on size and weight of certain organs in male white rat, 280.
Heymans, J. Y., *in vivo* as *in vitro* bacteria pass through the walls of filters, 255.
Hildebrandt, W., chronic lung disease following influenza, 297.

Hill, A. V., tetanic nature of voluntary contraction of human muscle, 530.
Hill, L., and McQueen, J. M., measurement of capillary blood-pressure in man, 166.
Hinman, F., diverticula of bladder, 184.
Hirai, K., formation of paraoxyphenylacetic acid and paraoxyphenylacrylic acid from laevo-tyrosin by bacteria, 473.
Hirsch, E. F., changes in leucocytes and alkali reserve of blood in experimental infections, 368.
Hirsch, E. F., rigor mortis in smooth muscle and a chemical analysis of fibromyoma tissue, 280.
Hitzenberger, K.: *see* Brunn, F., Hitzenberger, K., u. Saxl, P.
Hober, R., electromyogram in hemiplegia, 533.
Hoffmann, E., urticaria produced by flea-bites, 113.
Hoffmann, P., electromyogram in, and function of, tendon reflexes, 531.
Hoffmann, V., results of treatment of cancer of breast by excision and radiation, 422.
Hoffmann, W.. intestinal obstruction due to ascarides, 104.
Hofmann, F. B., theory of smell: parosmia, 281.
Holker, J., methods of measuring opacity of liquids, 580.
Holland, neurosyphilis, 60.
Holland, E., melanotic cancer of vulva, 233.
Hollande, A. Ch., formation of melanin in the blood of some insects, 230.
Hollo, J., experiments on source of variations in reaction of normal human urine, 385.
Holmes, A. D., and Deuel, H. J., jun., digestibility of some hydrogenated oils, 282.
Holmes, J. B., congenital obliteration of bile-ducts, 128.
Honeywell, H. E.: *see* Scott, E. L., and Honeywell, H. E.
Hooker, D. R., functional activity of capillaries and veins, 278.
Hopkins, F. G., auto-oxidizable constituent of cell, 573.
 effect of heat and aeration upon fat-soluble vitamine, 84.
 vitamine content of milk, 84.
Hoppe, E.: *see* Maltaner, F., and Hoppe, E.
Horiuchi, Y., studies on blood-fat. I. Variation of blood-fat constituents of rabbits under normal conditions. II. Lipaemia in acute anaemia, 88.
Hornowski, J.: *see* Rothfeld, J., Freund, J., u. Hornowski, J.
Hornus, P., amoebic dysentery in Morocco, 402.
Horsley, V.: *see* Spencer, W. G., and Horsley, V.
House, S. J., haemorrhagic meningo-encephalitis in anthrax: a report of three cases, 161.
Houzel et Sevestre, pulmonary gangrene cured by anti-gangrene serum, 316.
Howell, K. M., and Eby, H., tramission of specific immune bodies from mother to young, 164.
Hufnagel. L.: *see* Bergé, A., et Hufnagel, L.
Hume, E. M., comparison of growth-promoting properties for guinea-pigs of certain diets consisting of natural foodstuffs, 386.
 investigation of antiscorbutic value of full cream sweetened condensed milk by experiments on monkeys, 387.
Hunt, Reid, some factors relating to toxic action of arsphenamine, 580.
Huntemüller, epidemic of diphtheria in 19th Bavarian Infantry Regt., 18.
Hunter, W., Serbian epidemics of typhus in 1915, 191, 198.
Hurst, A. F., gastric and duodenal ulcers, 5.
 psychology of special senses and their functional disorders, 53.
 treatment of constipation, 221.
 treatment of duodenal ulcer, 14.
Hussey, H.: *see* Williams, A. W., Unneberg, A., Goldman, A., and Hussey, H.
Hussey, R. G.: *see* Murphy, J. B., Nakahara, W., Hussey, R. G., and Sturm, E.
Huston, J.: *see* Bunting, C. H., and Huston, J.
Hutinel, J.: *see* Labbé, M., et Hutinel, J.

Iancoresco, N.: *see* Widal, P., Abrami, P., et Iancoresco, N.
Iizuka, N.: *see* Aoki, K., u. Iizuka, N.
Imrie, C. G., and Graham, S. G., fat-content of embryonic livers, 88.
Irala, J., investigations on phagocytosis, 460.
Isaac, C. L., keratodermia blennorrhagica, 110.
Isaicu: *see* Levaditi, C., Marie, A., et Isaicu.
Ivens, F., serum treatment of gonorrhoea, 216.
Iversen, P., experiments upon distribution of phosphates between blood corpuscles and plasma *in vivo* and *in vitro*, 469.
Iyer, S. R., generalized vaccinia in Burmese children, 208.
Izar, G., acetone and diacetic acid in urine in pneumonia, 299.

Jacki, E., epidemic of Shiga bacillus dysentery in Heidelberg Children's Clinic, 400.
Jackson, H.: *see* Palmer, W. W., Salvesen, H., and Jackson, H.
Jackson, J. H., evolution and dissolution of nervous system, 141.
Jacobi, W., mental disturbances in tumours of the basal ganglia, 447.
Jacoby, A., treatment of gonorrhoea in women, 215.
Jacod, M., intracranial extension of sarcomata of Eustachian tube: syndrome of petro-sphenoidal junction, 242.
Jacquelin, A.: *see* De Jong, S. I., et Jacquelin, A.
Jager, R.: *see* Kolmer, J. A., Davis, L. C., and Jager, R.
Jagic, N., u. Schiffner, O., gonococcal infection of the heart, 211.
Jaksch-Wartenhorst, R., immunity against influenza, 304.
Jamin, F., u. Stettner, E., influenza in children, 303.
Janney, N. W., treatment of diabetes, 504.

Janney, N. W., and Newell, R. R., diabetes and tuberculosis, 500.
Janssen, H., diphtheria of mouth, 19.
Japiot, P., et Bussy, L., simplified technique for radiotherapy of eye, 583.
Jardet, parotid swelling due to denture, 3.
Jeans, P. C., treatment of congenital syphilis, 416.
Jeliffe, S. E., multiple sclerosis and psychoanalysis, 441.
Jennicke, E., dysentery epidemic in Thüringen, 399.
Jensen, J.: *see* Chievitz, O., Jensen, J., Reyn, A., and Collin, E.
Jephcott, H., and Bacharach, A. L., antiscorbutic value of dried milk, 387.
Joerdens, G., spontaneous pneumothorax, 319.
Johns, C. O., and Finks, A. J., studies in nutrition. V. Nutritive value of soy bean flour as supplement to wheat flour, 468.
Johnson, S. E., and Mason, M. L., first thoracic white ramus communicans in man, 446.
Joltrain, E., complement-fixation test for diagnosis of plague, 361.
de Jong, S. I.: *see* Bezançon, F., et de Jong, S. I.
De Jong, S. I., et Jacquelin, A., pleuritic hemiplegia, 319.
Jordan, E. O., and Sharp, W. B., effect of vaccination against influenza and some other respiratory infections, 564.
Jores, L., experimental investigations on influence of mechanical compression on bones, 369.
Jorge, R., typhus in Portugal, 193.
Joslin, E. P., frequency of diabetes in U.S.A., 498.
  obesity preceding diabetes, 503.
Josse, M. H., pulmonary radioscopy and radiography, 581.
Jotten, K. W., relative toxicity of different strains of *Gonococcus*, 210.

Kahn, M., angina pectoris in diabetic patients, 499.
Kalberlah, F., aetiology and disseminated sclerosis, 149.
Kaneko, R., u. Morihana, S., researches on identity of *Spirochaeta icterohaemorrhagiae* (Inado and Ito) and *Sp. icterogenes* (Uhlenhuth and Fromme) and the relation of *Sp. hebdomadis*, the cause of seven-day fever (Nanukayami), to *Sp. icterogenes*, 455.
Kantor, J. L., intra-intestinal treatment of hookworm infection, 107.
Karsner, H. T., and Swanbeck, C. E., removal of particulate matter from pleura, 462.
Kästner H., results of treatment of cancer of breast by excision and radiation, 422.
Kaufman, I., myelinization of posterior column of cord, 547.
Kausch, W., aneurysm of vertebral artery, 333.
Kaya, A., and Starling. E. H., effects of asphyxia on spinal animal, 429.
Kayser-Petersen: *see* Treupel u. Kayser-Petersen.
Kehrer, E., calcium content of blood in toxaemias of pregnancy, 543.
Keidel, A., and Moore, J. E., intraspinal treatment of neurosyphilis with salvarsanized serum, 339.
Keisman, M., splenogenous thrombopenia, 124.
Keith, A., function of large intestine, 222.
  *see* Spencer, W. G., and Keith, A.
Kellas, A. M.: *see* Haldane, J. S., Kellas, A. M., and Kennaway, E. L.
Kelley, M. F.: *see* Coca, A. F., and Kelley, M. F.
Kennaway, E. L.: *see* Gilliatt, W., and Kennaway, E. L.
  *see* Haldane, J. S., Kellas, A. M., and Kennaway, E. L.
Kepinow, L.: *see* Weinberg, M., et Kepinow, L.
Ker, C. B., intra-muscular route for injection of diphtheria antitoxin, 28.
Kersten, H. E., treatment of typhus by intravenous injections of collargol or 'fulmargin', 198.
Kestner, O., action of irradiation on blood-pressure, 278.
  active factor in high altitudes, 278.
Kieffer, O., pulmonary disease and influenza, 302.
Kiendl, W., use of tuberculin and quinine in lupus erythematosus, 112.
Kiessling, W., comparative experiments upon the effect of some chlorine derivatives of methane, ethane, and ethylene upon isolated frog's heart, 472.
King, W. G., vaccination in the tropics, 207, 208.
Kipp, H. A., variation in cholesterol content of serum in pneumonia, 87.
Kirby, G. H., and Davis, T. K., psychiatric aspects of epidemic encephalitis, 447.
Kirch, A., enlarged mediastinal glands in influenza, 298.
Kirmisson, E., anterior dislocation at elbow, 42.
Kissmeyer, A., effects of light baths on vitiligo, 111.
Kleberger, K., pneumonomycosis aspergillina after influenza, 298.
Kleeblatt, F., indications for splenectomy, 124.
de Kleijn, A., tonic labyrinthine and neck reflexes of eyes, 151.
de Kleijn, A., u. Magnus, R., functions of the otoliths. I. The place of otoliths in tonic labyrinth reflexes. II. Separate removal of otoliths in the guinea-pig, 152.
  labyrinthine reflexes to progressive movements, 151.
Kleinschmidt, K., diathermy in treatment of whooping-cough, 203.
Kleitmann, N.: *see* Scott, E. L., and Kleitmann, N.
Klemperer, G., influenzal nephrosis, 299.
Koch, H., rashes in diabetic children, 500.
Kocher, A., anterior dislocation at elbow, 41.
Kodama, R., ocular reactions in anaphylaxis, 164.

Koettlitz, H., primary sarcoma of stomach, 9.
Kofman : *see* Cluzet, Rochaix, et Kofman.
Kohda, K., cultivation of *B. leprae*, 558.
Kolmer, J. A., Davis, L. C., and Jager, R., influence of chaulmoogra oil on tubercle bacillus, 262.
Kongsted, E., comparative value of methods of Herman and Ziehl-Neelsen for staining tubercle bacilli, 83.
Kop, W. A. : *see* Hehewerth, F. H., and Kop, W. A.
Korbsch, R., u. Gross, A., vaccine treatment of dysentery, 404.
Kossel, A., u. Giese, G., colouring matter in chloroma, 579.
Kowallek, A., plethysmographic investigations on effects of high-frequency currents, 279.
Kraft, A., haemolytic streptococci of appendix vermiformis, 257.
de Kraft, F., action of electric currents on endocrine glands and other tissues, 99.
Kramer, P. H., importance of lice in transmission of typhus, 194.
  epidemic of typhus in Rotterdam, 1919, 192.
  incubation period of typhus, 192.
Kreuter, E., osteochondritis deformans juvenilis coxae, 39.
Krogius, A., studies in genesis of Dupuytren's contraction, 52.
Kroh, F., injury causing spasmodic contraction of arteries, 35.
Kromayer, E., diphtheria of vulva, 20.
de Kruif, P. H., dissociation of microbic species. I. Coexistence of individuals of different degrees of virulence in cultures of bacillus of rabbit septicaemia, 568.
Krumbhaar, E. B., and Masser, J. H., jun., studies of the blood of normal monkeys, 572.
Krumwiede, C. : *see* Park, W. H., Williams, A. W., and Krumwiede, C.
Kunstmann, erythromelalgia, 113.
Küntzel, O., tar cancer, 114.
Kuramitsu, C., and Loeb, L., involution of uterus following labour, and influence of castration and suckling on process of involution, 474.
  effect of suckling and castration on lactating mammary gland in rat and guinea-pig, 474.
Küttner, H., gunshot wound of vertebral artery, 330.
Küttner, H., u. Baruch, M., injury causing spasmodic contraction of arteries, 33, 36.

Labbé, M., diabetic epilepsy, 499.
Labbé, M., et Hutinel, J., two cases of typhus in Paris, 193.
Labouré, J., injury to external carotid during removal of tonsils, 327.
Ladwig, B. : *see* Borchardt, L., u. Ladwig, B.
Lafaye, A., treatment of infantile syphilis with intravenous injections of neosalvarsan, 415.
  value of luetin reaction in diagnosis of congenital syphilis, 412.
Lakaye, neurosyphilis after regular and sufficient arsenical treatment in primary stage, 336.
Lane, C., ankylostomiasis in Darjeeling district, 106.
Lane, W. A., surgical treatment of intestinal stasis, 221.
Langelaan, J. W., muscle tonus, 532.
Langfeldt, G., blood-sugar regulation and origin of hyperglycaemias. I. Glycogen formation and glycogenolysis. II. Conditions of action of liver diastases. III. Theory, 470.
Lantin, P. T.: *see* Haughwout, F. G., and Lantin, P. T.
Lanzilotta, R., use of ultra-violet rays in the preparation of vaccines, 356.
Lambert, diphtheria of middle ear, 19.
Lapin, J., et Senevet, G., Weil-Felix reaction in typhus, 197.
Laquerrière : *see* Delherm et Laquerrière.
Laqueur, E., and Magnus, R., experimental pathology and therapy of phosgene poisoning, 384.
Laska-Mintz, E.: *see* Parnas, J. K., u. Laska-Mintz, E.
Lauenstein, R., treatment of injuries to vertebral artery, 332.
de Laulerie : *see* Ribadeau-Dumas, Mallet, et de Laulerie.
Laura, C. L., serum treatment of diabetes, 507.
Lauritzen, M., treatment of diabetes, 504, 506.
De Lavergne, diphtheritic paralysis, 24.
  *see* Besson, A., et de Lavergne.
De Lavergne et Zoeller, Shick test of susceptibility to diphtheria, 26.
Läwen, A., u. Reinhardt, A., oxyuriasis of appendix, 105.
Le Bon, G., certain antagonistic properties in different regions of spectrum, 396.
Lecéne, P., et Lhermitte, J., cerebral softening from metallic embolus in left middle cerebral artery, 251.
Lederer, K., pseudo-membranous oesophagitis, 299.
Lederer, R., painting throat with solution of silver nitrate in treatment of pertussis, 203.
Leendertz, G., diphtheria of vagina and skin of intragluteal folds, 20.
Leete, H. M., Shick test for susceptibility to diphtheria, 26.
Lefeuvre : *see* Marquis et Lefeuvre.
Legg, A. T., non-tuberculous juvenile coxalgia, 38.
Legrand, H., multiple amoebic abscesses, 403.
Legrand et Auguste, C., seropurulent effusion in pleura in influenzal pneumonia, 298.
Legry, Courcoux, et Lermoyez, J., outbreak of mild typhus in a home for foreign workmen in Paris, 193.
Lehmann u. Scheven, results of treatment of cancer of breast by excision and radiation, 422.
Leimdörfer, A., skin eruptions in influenza, 300.

Lemann, I. I., case of Shiga bacillus dysentery with pseudo-membrane in vagina, and oedema of abdominal wall, 402.
Lemon, W. S., angioma of stomach, 10.
Lenhardt, C. H.: *see* Marine, D., and Lenhardt, C. H.
Lennhoff, C., inoculation for psoriasis, 110.
Lenormant, C., cutex verticis gyrata, 114.
  diffuse sclerosis of skin and of cellular tissue of neck following prolonged radiotherapy: cicatricial torticollis, marked oedema of face, laryngotracheal compression, 391.
  gas cysts of intestine, 11.
de Léobardy, J.: *see* Agulhon et de Léobardy, J.
  *see* Ribierre, P., et de Léobardy, J.
Leriche, R., et Heitz, J., injury causing spasmodic contraction of arteries, 33.
Lermoyez, J.: Legry, *see* Courcoux, et Lermoyez, J.
Levaditi, C., et Harvier, P., experimental study of lethargic encephalitis, 148, 262.
Levaditi, C., Marie, A., et Isaicu, researches on spontaneous spirochaetosis of rabbit, 569.
Levene, P. A., and Rolf, I. P., lecithin of brain, 473.
Levin, I.: *see* Cohen, M., and Levin, I.
Levy, C. S., congenital absence of a lung, 309.
Lévy, P. P., interpretation of blood-cultures, 458.
Lévy-Bing, A., et Duroeux, L., arsenical compounds in treatment of gonorrhoeal salpingitis, 216.
Lévy-Franckel, A., splenomegaly following injection of neosalvarsan, 122.
Lewis, D. S., and Mason, E. H., diastatic ferments of blood, 87.
Lewis, H. B.: *see* Stearns, G., and Lewis, H. B.
Lewis, W. H., and Webster, L. T., giant cells in cultures from human lymph nodes, 370.
Lewy, F. H.: *see* Cassirer, R., u. Lewy, F. H.
Lhermitte, J.: *see* Lecéne, P., et Lhermitte, J.
Lian, C., et Cathala, J., vagotonia in asthma, 312.
Lichtenstein, A., pyloric spasm, 7.
Lichtenstein, S., case of spontaneous tuberculosis in frog, 84.
Lieben, F.: *see* Fürth, O., u. Lieben, F.
Liebhardt, E., demonstration of active tuberculosis by Wildbolz's auto-urine reaction, 559.
Liljestrand, G., u. Magnus, R., physiology of muscular spasm in tetanus, 533.
Lilly, T. E., Schick test for susceptibility to diphtheria, 25.
Lindburg, G., post-traumatic serous meningitis in children, 253.
Lindstedt, F., contribution to pathogenesis of sciatica, 254.
Linzenmeier, G., investigations on rate of sedimentation of red blood corpuscles, 175, 543.
Litch, V. M., and Meyer, K. F., spontaneous epidemic among laboratory rabbits caused by paratyphoid B bacillus related to rodent group, 80.
Lloyd, J. H., syphilis of eighth nerve, 447.
Loeb, L.: *see* Kuramitsu, C., and Loeb, L.
Loeb, L., and Kuramitsu, C., influence of lactation on sexual cycle in rat and guinea-pig, 475.
Loeper, M., Forestier, J., et Tonnet, J., paradoxical hyperalbuminosis in blood of cancer subjects, 466.
Loewenhardt, F. E. R., aetiology of influenza, 155.
Löffler, W., liver function under experimental pathological conditions, 542.
  *see* Bloch, Br., u. Löffler, W.
Logan, W. R.: *see* Cranston Low, R., Logan, W. R., and Rutherford, A.
Loisleur, J., pulmonary gangrene cured by artificial pneumothorax, 316.
Lomholt, S., prostitution and alcohol in causation of gonorrhoea, 210.
Looft, C., diphtheria in the new-born, 21.
  umbilical diphtheria, 22.
Lord, F. T., pulmonary abscess, 315.
Lortat-Jacob, cryocautery, 114.
  influenza in old pleuritics, 302.
Losee, J. R., and van Slyke, D., toxaemias of pregnancy, 537 et seq.
Losio, L., haemolytic jaundice with splenomegaly, 123.
Lotsch, F., osteo-myelitis of hyoid after influenza, 301.
Loughlin, R.: *see* Daniels, A. L., and Loughlin, R.
Low, G. C., diagnosis of dysentery, 403.
Lowe, E. C., membranous colitis in influenza, 299.
Löwy, R., a typical typhus, 194.
Lüain, M., reflex gastrospasm, 129.
Lubarsch, O., melanotic cancer in animals, 233.
Lubinski, H., bacteriology of wound diphtheria, 162.
Luccarelli, V., war splenomegaly, 121.
Lüers, N., general colloid test in cerebrospinal fluid and use of Congorubin, 479.
Lumière, A., et Chevrotier, J., simple and harmless method of preventing anaphylactic shock, 458.
Lundegaard, K. K. K., universal light baths in ophthalmology, 346.
Lusk, G., production of fat from protein, 86.
Lynch, V., chemistry of whitefish sperm, 89.
Lyon, R. H.: *see* Beckwith, T. D., and Lyon, R. H.
Lyter, J. C., non-tuberculous lung infection, 314.

Maalöe, C. U., practical value of Elsner's gastroscopy, 439.
McCann, W. S., observation of effect of protein meal given to a man at end of 8-day fast, 86.
McCarty, E. D.: *see* McClure, C. W., and McCarty, E. D.
Maccarty, W. C., pathological changes in 4,998 removed gall-bladders, 126, 128.
McCaskey, D., quartz ultra-violet therapy and kinetic energy, 391.
Macchi, A.: *see* Zenoni, C., e Macchi, A.

McClure, C. W., and McCarty, E. D., roentgenographic studies in gout, 484.
McCollum, E. V., Simmonds, N., Parsons, H. T., Shipley, P. G., and Park, E. A. I. Production of rachitis and similar diseases in the rat by deficient diets. II. Effect of cod-liver oil administered to rats with experimental rickets, 176.
McConnell, A. A., fatal case of splenectomy for cirrhosis of liver, 124.
McDonagh, J. E. R., varieties of ulcus molle, 218.
  treatment of ulcus molle, 220.
Macdonald, E. L.: *see* Alexander, M. E., and Macdonald, E. L.
McFarland, J.: *see* Deaver, J. B., McFarland, J., and Herman, J. L.
Macht, D. I., benzyl benzoate in treatment of whooping-cough, 203.
McIntosh, J., transmission of experimental encephalitis lethargica in series in monkeys and rabbits, with notes on spontaneous infection in monkey, 65.
McJunkin, F. A., tuberculin hypersensitiveness in non-tuberculous guinea-pigs induced by injections of bacillus-free filtrates, 558.
Mackay, H. M. M., effect on kittens of a diet deficient in animal fat, 386.
Mackenzie Wallis, R. L., toxaemias of pregnancy, 540.
McKhann, C. F.: *see* Rockwell, G. E., and McKhann, C. F.
McKibben, P.: *see* Weed, L., and McKibben, P.
Mackie, T. J., and Rowland, C. C., value of simultaneous testing for Wassermann reaction with two different antigens and 'ice-box method', 58.
McLean, F. C., Murray, H. A., jun., and Henderson, L. J., variable acidity ot haemoglobin and distribution of chlorides in blood, 88.
McLean, S., intestinal parasites in young children in New York, 103.
MacLeod, C.: *see* Rolleston, J. D., and MacLeod, C.
MacLeod, J. J. R., concentration of lactic acid in blood in anoxaemia and shock, 376.
  periodic breathing and effects of oxygen administration in decerebrate cats, 383.
McMurray, T. E., benzyl benzoate in treatment of whooping-cough, 203.
McQueen, J. M.: *see* Hill, L., and McQueen, J. M.
Magner, W., complement-fixation test for gonorrhoea, 212.
Magnus, R., choline, hormone of intestinal peristalsis, 479.
  *see* de Kleijn, A., u. Magnus, R.
  *see* Laqueur, E., and Magnus, R.
  *see* Liljestrand, G., u. Magnus, R.
Maisonneuve et Favrat, ligation of vertebral artery, 330.
Maitland, H. B., Cowan, M. L., and Detweiler, H. K., aetiology of epidemic influenza: experiments in search of filter-passing virus, 67.
Maitland, H. B., Cowan, M. L., and Detweiler, H. K., spontaneous and artificial pulmonary lesions in guinea-pigs, rabbits, and mice, 154.
Makins, G. H., aneurysm and cerebral embolism following gunshot injury, 328.
  arteriovenous aneurysm, 322.
Mallet: *see* Ribadeau-Dumas, Mallet, et de Laulerie.
Mallory, W. J., amoebic dysentery, 402.
Malone, J. Y.: *see* Sachs, E., and Malone, J. Y.
Maltaner, F., and Hoppe, E., chemotactic effect of osmosis upon leucocytosis, 362.
  osmosis as factor in local accumulation of leucocytes in body, 90.
Mandlebaum, F. S., and Downey, H., histopathology of Gaucher's disease, 120.
Manini, L., treatment of amoebic abscess of liver, 404.
Manoukhin, I. I., treatment of infectious diseases by leucocytolysis produced by röntgenization of spleen, 485.
Manson-Bahr, P., monarthritis or polyarthritis as complication of bacillary dysentery in Egypt and Palestine, 400.
Marfan, A. B., asthma in children, 311.
Marie, A.: *see* Levaditi, C., Marie, A., et Isaicu.
Marie, P. L.: *see* Armand-Delille, P. F., et Marie, P. L.
Marine, D., and Lenhart, C. H., effects of adrenalin on respiratory exchange, 274.
Marquis et Lefeuvre, anastomosing current after ligature of common carotid, 329.
Marriott, W. M., post-diphtheritic paralysis of respiratory muscles, 24.
Marsh, P. L.: *see* Newburgh, L. H., and Marsh, P. L.
Marshall, E. K.: *see* Rowntree, L., Chesney, A. M., and Marshall, E. K.
Martin, L., antitoxin treatment of diphtheria, 27.
Martindale, L., intensive X-ray therapy versus hysterectomy for fibromyomata of uterus, 95.
Mason, E. H.: *see* Lewis, D. S., and Mason, E. H.
Mason, F. R., ipecac sensitization and bronchial asthma, 310.
  treatment of bronchial asthma with benzyl benzoate, 312.
Mason, M. L.: *see* Johnson, S. E, and Mason, M. L.
Mason, V. R., bronchial spirochaetosis, 313.
Masser, J. H., jun.: *see* Krumbhaar, E. B., and Masser, J. H., jun.
Mas y Magro, F., blood picture in anaphylaxis, 358.
Matas, R., aneurysm of vertebral artery, 330.
Mathieu, P., cholecystogastrotomy, 131.
Mathison, G. C., action of asphyxia on spinal animal, 429.
Matsumoto, M., experiments upon the production of antihuman haemolysin with special reference to immunization with erythrocytes sensitized with heated serum, 165.
Matsunaga, T., diffuse pigmentation in melanotic cancer, 233.

Matthew, D.: *see* Rixon, C. H. L., and Matthew, D.
Matthiasson, S., influenza epidemic in Iceland, 296.
Mattill, P. M., Mayer, K., and Sauer, L. W., influence of intravenous injections of acacia-glucose solutions on urine excretion and blood-volume in rabbits, 277.
Mattirolo, G., e Bertolotti, M., rare malformation of cephalic end of vertebral column, 370.
Mauelshagen, F.: *see* Habermann, R., u. Mauelshagen, F.
May, E.: *see* Widal, F., et May, E.
Mayer, K.: *see* Mattill, P. M., Mayer, K., and Sauer, L. W.
Mayer, L., acute haematorrhagic pancreatitis with necrosis, 510.
Mayer, M., examination of blood and stools of coloured prisoners of war, 105.
Mayo, C. H., union of hepatic duct with duodenum, 131.
  mortality from cholecystectomy, 126.
Mayo, W. J., splenic anaemia, 119.
Mead, S. W.: *see* Dutiker, R. A., Eckles, C. H., Dahle, C. H., Mead, S. W., and Schaefer, O. G.
Meader, P. D.: *see* Robinson, G. H., and Meader, P. D.
Meader, P. D., and Robinson, G. H., biological and physical properties of haematoxin of streptococci, 69.
Meek, W. J., and Eyster, J. A. E., reactions to haemorrhage, 470.
Megaw, J. W. D., hookworm infection in United Provinces of India, 106.
Meier, K.: *see* Straub, H., u. Meier, K.
Melman, R. J., tabes mesenteria following influenza, 302.
Ménard, pregnancy after radiotherapy for fibroid, 95.
Mendel, L. B.: *see* Osborne, T. B., and Mendel, L. B.
Mengert, E., silver-salvarsan in treatment of congenital syphilis, 416.
Menninger, K. A., influenza and hypophrenia, 300.
Mensching, H., results of vaccination of 684 infants in Obstetrical Institute at Hamburg, 206.
Menten, M. L., variations in benzidin peroxidase reaction depending on fixative, physiological activity, and type of animal, 68.
Mercadé, S., end to end ileo-sigmoidostomy, 140.
Merk, L., Recklinghausen's disease, adenoma sebaceum, and tuberous sclerosis caused by infection with some dicotyledonous plant, 114.
Metalnikow, S., on natural and acquired immunity in larva of *Galleria mellonella*, 82.
Metchnikoff, É., function of large intestine, 222.
Meyer, A. H., report of whooping-cough investigations at State Serum Institute at Copenhagen, 561.
  diphtheria prophylaxis, 26.
Meyer, A. W., toxic effects of injection of novocaine and bicarbonate solution into a vein, 518.
Meyer, B. I.: *see* Gray, G. A., and Meyer, B. I.
Meyer, H., non-specific horse serum in treatment of diphtheria, 28.
  *see* Frohlich, A., u. Meyer, H.
Meyer, K. F.: *see* Litch, V. M., and Meyer, K. F.
Mhaskar, K. S., hookworm infection in Tanjore, Trichinopoly, Madura, and Ramnad, 106.
  *see* Caius, J. F., and Mhaskar, K. S.
Michon, L.: *see* Forestier, J., et Michon, L.
Miescher, G., malignant melanoma of skin, 234.
Mignot, R.: *see* Rénon, L., et Mignot, R.
Milani, E., bactericidal action of secondary rays from colloidal metals, 94.
Milio, G., blood in influenza, 297.
Miller, D. A.: *see* Young, J., and Miller, B. A.
Miller, R., and Perkins, H., congenital steatorrhoea, 509.
Ministry of Health, report on influenza pandemic of 1918–19, 296.
Mishulow, L.: *see* Cooper, G. M., Mishulow, L., and Blanc, N. E.
Mitchell, J. W.: *see* Allen, F. M., Mitchell, J. W., and Sherrill, J. W.
Montgomery, D. W., and Culver, G. D., eczema of vermilion border of lips, 111.
Moog, O., u. Wörner, E., *Trichocephalus trichiurus* in soldiers, 107.
Moore, J. E.: *see* Keidel, A., and Moore, J. E.
Moore, R. F., melanoma and melanotic cancer of eye, 235.
Moorhead, T. G., myelitis in dysentery patient, 402.
Montel, L. R., local application of anti-streptococcic serum in treatment of chronic sepsis of skin, 111.
Monziols et Collignon, treatment of typhus with iodized *Proteus* X 19 vaccine, 199.
Morenas: *see* Bonnet, L. M., et Morenas.
Morihana, S.: *see* Kaneko, R., u. Morihana, S.
Moro, E., sudden death in eczema, 111.
Morrison, L. F.: *see* Gay, F. P., and Morrison, L. F.
Morriston Davies, H.: *see* Trotter, W., and Moriston Davies, H.
Mosenthal, H. O., and Wiener, H. J., dietetic treatment of diabetes, 505.
Moszeik, lethargic encephalitis following typhus, 195.
Mott, F., CO poisoning, 430.
Mott, F. W., symptoms of syphilis in cases of juvenile general paralysis and tabes, 412.
Mottram, J. C., red cell content of those handling radium for therapeutic purposes, 93.
  histological changes in bone-marrow of rats exposed to γ-radiations from radium, 93.
  *see* Cramer, W., and Mottram, J. C.
Mouchet, A., inflammation of tarsal scaphoid in young children (Köhler's disease), 483.

Mouchet, A., infantile osteo-chondritis deformans of upper epiphysis of femur, 481.
Mouriquand, G., et Bertoyo, trichocephaliasis with severe anaemia and diarrhoea, 108.
Mueller, J. H., bacterial metabolism, 90.
Müller, E. F., fatal cases of influenza complicated by infection with *Aspergillus fumigatus*, 298.
Müller, H., treatment of gonorrhoea by intramuscular injections of turpentine and 'aolan', 214.
Müller, S., enterostomy for post-operative intestinal obstruction, 440.
Muraud, J., treatment of acute suppuration of wrist, 237.
Murphy, J. B.: *see* Nakahara, W., and Murphy, J. B.
Murphy, J. B., Hussey, R. G., Sturm, E., Nakahara, W., effect of induced cellular reaction on fate of cancer grafts, 488.
Murphy, J. B., Nakahara, W., Sturm, E., relation between time and extent of lymphoid stimulation induced by physical agents and degree of resistance to cancer in mice, 489.
Murphy, J. B., Nakahara, W., Hussey, R. G., Sturm, E., effect of cellular reaction induced by X-rays on cancer grafts, 488.
Murray, H. A., jun.: *see* McLean, F. C., Murray, H. A., jun., and Henderson, L. J.
Murstad, E., Sachs-Georgi syphilis reaction, 361.
Musumeci, G., e Di Macco, G., insensible perspiration through cutaneous scars and skin of paretic limbs, 370.

Naccarati, S., oculo-cardiac reflex (Dagnini-Aschner phenomenon)—its use in medicine and psychology, 150.
Naessens, subcutaneous injections of oxygen in treatment of influenzal bronchopneumonia, 305.
Nagao, K., fate of india ink injected into blood, 171.
Nageotte, J., et Sencert, L., grafts of dead tendon, 527.
Nakahara, W.: *see* Murphy, J. B., Nakahara, W., Hussey, R. G., Sturm, E.
Nakahara, W., and Murphy J. B., influence of cancer inoculation on lymphoid stimulation induced by small doses of X-rays, 489.
  effect of small doses of X-rays of low penetration on resistance of mice to transplanted cancer, 489.
Nanta, A., et Baudru, L., lymphadenoma with pruritus, 114.
Nasso, I., spasmodic sneezing in whooping-cough, 201.
Nathan, E., production of antibodies in trichophytic infection, 112.
Naunyn, B., relation of jaundice to revaccination, 209.
Neal, H. V., nerve and plasmodesma, 445.
Neame, H., treatment of interstitial keratitis due to congenital syphilis, 411.
Negelein, E.: *see* Warburg, O., u. Negelein, E.
Neher, R., results of treatment of cancer of breast by excision and radiation, 422.
Neilson, I. L.: *see* Waite, J. H., and Neilson, I. L.
Neri, V., semeiological importance of electrical examination of cutaneous sensibility, 490.
Netter, A., et Salanier, M., case of typhus contracted in Poland, 193.
Neugebaur, volvulus of sigmoid flexure, 227.
Neuberg, C., Nord, F. F., u. Wolff, E., acetaldehyde as intermediary substance in fermentation of sugar by *B. lactis aerogenes*, 388.
Neuber, E., gastric myomata, 10.
Neubürger, K., post-mortem pigmentation of skin, 112.
Neuda, P., syphilis and influenza, 302.
Neudörfer, A., treatment of volvulus of sigmoid flexure, 227.
Neumann, J., u. Zoepffel, H., diaphragmatic pleurisy in influenza simulating perforative peritonitis, 301.
Neumann, M., helminthiasis in infants, 103.
Nevin, Mary, botulism from cheese, 353.
Nevin, M.: *see* Williams, A. W., Nevin, M., Gurley, C. R.
Newburgh, L. H., and Marsh, P. L., dietetic treatment of diabetes, 506.
Newell, R. R.: *see* Janney, N. W., and Newell, R. R.
Nicolaysen, K., irritation of vagus and haemorrhagic erosions of stomach, 5.
Nicolaysen, N. A., case of rat-bite fever, 271.
Nicoll, J. H., chronic pancreatitis, 510.
Nicolle, C., et Conseil, E., use of serum of typhus convalescents in prophylaxis of typhus, 197.
  prophylactic vaccination against Malta fever, 256.
Nicolle, C., et Cuénod, A., experimental trachoma, 462.
Ninni, C., a new anaerobic soil bacillus (*B. spermoides*), 160.
  size of spores of soil bacteria, 159.
  on flora of small intestine of small herbivora, with special reference to presence in it of *B. coli*, 76.
Nitch, C. A. R., and Shattock, S. G., diffuse emphysema of intestinal wall, 10.
Nogier, T., radium therapy for uterine fibroids, 285.
Noiré, H., precautions to be taken in X-ray therapy of ringworm, 112.
Nonne, M., myeloma of spine, 250.
Nonnenbruch, blood after administration of urea, 277.
Nord, F. F.: *see* Neuberg, C., Nord, F. F., u. Wolff, E.
Novak, E., polypoid adenoma of stomach, 10.
Novaro, P., calorimetric investigations on inanition and deficiency disease, 167.
  changes in the interstitial tissue of testicle in consequence of deficiency in water-soluble accessory substance B, 168.

O'Donovan, W. J., dermatitis due to *Carpoglyphus passularum* in persons handling figs, 113.
  tar cancer, 113.
Oehme, C., secretion of water by kidney in relation to general water metabolism, 575.
Offenbacher, R., investigations into the activity of pulmonary tuberculosis by Wildbolz's method, 559.
Okinczye, J., volvulus of sigmoid flexure, 227.
Olitsky, P. K., and Gates, F. L., experimental studies of nasopharyngeal secretions from influenza patients. I. Transmission experiments with nasopharyngeal washings. II. Filterability and resistance to glycerol. III. Studies in concurrent infections, 266. IV. Anaerobic cultivation, 560.
Olitsky, P. K.: *see* Amoss, H. L., Gates, F. L., and Olitsky, P. K.
Olitsky, P. K.: *see* Gates, F. L., and Olitsky, P. K.
Olmer, D., et Berthier, determination of volume of pleural cavity in course of pneumothorax, 571.
Olsen, O., action of blood in growth of influenza bacillus, 156.
Ornstein, M., bacteriology of bacillus of Schmitz, 78.
Osborne, T. B., and Mendel, L. B., critique of experiments with diets free from fat-soluble vitamine, 177.
  growth of diets poor in true fats, 177.
  ophthalmia and diet, 574.
Osgood, H. A., X-ray interpretation of gastro-intestinal tract, 389.
Otelesco, I.: *see* Weinberg, M., et Otelesco, I.
Otsubo, T., action of certain salts on phagocytosis and virulence of streptococci, 361.

Pallin, G., anatomical variation of bile-ducts, 126.
  malignant disease involving bile-ducts, 129.
Palmén, A. J., case of rat-bite fever in Helsingfors, 271.
Palmer, W. W., Salvesen, H., and Jackson, H., relationship between plasma bicarbonate and urinary acidity following the administration of sodium bicarbonate, 173, 539.
Palmer, W., and van Slyke, D., relation between alkali retention and alkali reserve, 539.
Palugyay, J., Röntgen observations on anatomy and physiology of cardia, 388.
Panayotatou, A., treatment of amoebic abscess of liver, 404.
Pannett, C. A., and Wilson, C. M., influence of bile salts on gastric function, 465.
Paraf, J., transmission of dysentery by flies, 399.
Pardi, U., action of concentrated sera, 166.
Park, E. A.: *see* McCollum, E. V., Parsons, H. T., Shipley, P. G., and Park, E. A.
Park, L. K.: *see* Eiskamp, E. H., and Park, L. K.
Park, W. H., duration of immunity from diphtheria, 26.
  *see* von Sholly, A. I., and Park, W. H.
Park, W. H., and Cooper, G., accidental inoculation of influenza bacilli on mucous membranes of healthy persons with development of infection in at least one. Persistence of type characteristics of bacilli. 267.
Park, W. H., Williams, A. W., Krumwiede, C., microbial studies on acute respiratory infection, with especial consideration of immunological types, 267.
Parker, G. H., elementary nervous system, 141, 144.
Parker, H. L., juvenile tabes, 149, 411.
Parnas, J. K., carbohydrate metabolism of isolated amphibian muscle, 577.
Parnas, J. K., u. Laska-Mintz, E., influence of subminimal stimuli upon the course of chemical changes in muscle, 577.
Parrino, G., experimental investigations on phagocytosis. Influence of various fixing agents, 171.
Parsons, H. T.: *see* McCollum, E. V., Simmonds, N., Parsons, H. T., Shipley, P. G., and Park, E. A.
Paterson, D. H., transmission of syphilis to third generation, 412.
Paton, D. N., and Watson, A., aetiology of rickets, 465, 574.
Patzschke, W., treatment of gonorrhoeal vulvo-vaginitis in children, 217.
Paul, E., splanchnic anaesthesia for gastric operations, 524.
Paulian, D. E., Marinesco's technique for intra-spinal treatment of neurosyphilis with salvarsanized serum, 337.
Paullin, J. E., renal glycosuria, 502.
Pawlow, I., 'conditional' reflexes, 428.
Payr, E., constipation and its surgical treatment, 222.
Pearce, L.: *see* Brown, W. H., and Pearce, L.
Pech, phenomena of antagonism between different rays (ultra-violet, visible spectrum, infra-red), 395.
Peiper, diphtheria of penis and umbilicus in new-born infant, 23.
  vulvar and cutaneous diphtheria, 20.
Perkins, H.: *see* Miller, R., and Perkins, H.
Permar, H. H., experimental study of mononuclear phagocytes of lung, 462.
Pernet, G., post-vaccinal psoriasis, 208.
Perrin-Maréchal, A., pulmonary abscess due to pneumobacillus, 315.
Perthes, G., arteriovenous aneurysm, 331.
  arthritis deformans juvenilis, 39.
  ligature of arteries, 329.
  results of treatment of cancer of breast by excision and radiation, 422.
Peshkin, M. M., ipecac sensitization and bronchial asthma, 310.
Peters, J. P., jun., and Barr, D. P., carbon dioxide dissociation curve and arterial and venous carbon dioxide tension of human blood in health and in disease, 173.
  respiratory mechanism in cardiac dyspnoea, 382.

Peters, J. P., Barr, D. P., and Rule, F. D., carbon dioxide absorption curve and carbon dioxide tension of blood of normal resting individuals, in cardiac dyspnoea, and in severe anaemia, 381.
Peters, V. J. W., pulmonary abscess, 314, 315.
Peterson, W. H. : *see* Fred, E. B., and Peterson, W. H.
Petow, H. : *see* Rona, P., u. Petow, H.
Petrén, K., mortality from 1918 epidemic of influenza in Sweden, 296.
  renal affection in influenzal pneumonia, 299.
Pette, H., relation of neurosyphilis to previous treatment, 335.
Petzétakis, D., parabronchial pleurisy, 318.
Peyron : *see* Alezais et Peyron.
Pézard, A., numerical law of regression of certain sex characters, 179.
Pfeiffer, R., right hemiplegia in typhus, 195.
Phillips, C. E. S., suggested new method of measuring X-ray dosage, 182.
Piccininni, F., epidemiological and anatomopathological observations on rat plague. Experimental investigations on immunity of rats against plague, 459.
  means of importation of plague into Italy and preventive measures, 459.
Pickering, D. V., blood-sugar in diabetes, 502.
Pighini, G., chemical composition of brain in dementia praecox, 479.
Pinch, A. E. H., report of work carried out at Radium Institute, London, from Jan. 1, 1919, to Dec. 31, 1919, 96.
Piñol, E. L., bronchial spirochaetosis, 313.
Piper, I. H., nature of electromyogram, 530.
Pirondini, E., pyelitis larvata cystalgica, 240.
Pistocchi, G., on influence of spleen, kidney, and thyroid on anaphylactic shock, 169.
Plaut, H. C., salvarsan in treatment of pulmonary gangrene, 316.
Plesch, J., inhalations of iodine vapour in prophylaxis of influenza, 304.
Plichet : *see* Weil, P. E., et Plichet.
Plimmer, R. H. A., analyses and energy values of foods, 573.
Pontano, T., treatment of amoebic abscess of liver, 403.
Ponticaccia, L., experimental investigations on haemolytic action of oleic acid and trioleins in rabbits, 166.
Porte : *see* Cristol et Porte.
Poulton, E. P. : *see* Haldane, J. S., and Poulton, E. P.
Povitsky, O. R., and Denny, H. T., further studies on grouping of influenzal bacilli, with special reference to permanence of type in carrier, 267.
Pozerski, E. : *see* Blanc, J., et Pozerski, E.
Pozzo, A., 'Norwegian scabies,' 113.
Prausnitz, C., bacteriology of swine erysipelas in man, 352.
Prausnitz, P. G., umbilical diphtheria, 22.
Preisendorf, F., function of tendon reflexes, 531.
Preiss, G. A., action of paravertebral injections in producing spinal anaesthesia, 523.
Price-Jones, C., diurnal variation in sizes of red blood cells, 366.
Pritchett, T. W. : *see* Wishart, M. B., and Pritchett, T. W.
Probizer, G., pellagra in the Trentino, 113.
Proust, R., et Ramond, L., empyema caused by rupture of amoebic abscess of liver, 403.
Prym, O., liability of diabetics to flea-bites, 500.
Pulido, A., recent outbreaks of typhus in Spain, 192.
Puntoni, V., tobacco smoke as disinfectant of the mouth, 357.
Putnam, T. J. : *see* Foley, F. E. B., and Putnam, T. J.
Putnam, J. J., and Gay, D. M., behaviour of influenza bacillus in mixed culture on haemoglobin-free media, 156.

Quick, D., results of treatment of cancer of breast with X-rays and radium after excision, 420.
  *see* Bagg, H. J., Ewing, J., and Quick, D.

Radin, M. J., chronic lung disease following influenza, 297.
Ragoff, J. M. : *see* Stewart, G. N., and Ragoff, J. M.
Rahnenfuhrer, C., clinical history of circumscribed pulmonary suppuration (abscess gangrene), 581.
Ramirez, M. A., horse asthma following blood transfusion, 311.
  protein sensitization in eczema, 111.
Ramond, F., pyloric spasm, 6, 184.
Ramond, F., et Clément, R., pylorospasm, 6.
Ramond, L. : *see* Proust, R., et Ramond, L.
Randall, S. B. : *see* Foster, L. F., and Randall, S. B.
Ransohoff, J., aneurysm of internal carotid due to peritonsillar abscess, 325.
Ransom, B. H., *Ascaris lumbricoides* causing pulmonary disease, 104.
Ransom, F. : *see* Dixon, W. E., and Ransom, F.
Rappleye, W. C. : *see* Forbes, A., and Rappleye, W. C.
Rathery, F., et Binet, L., saliva in diabetic patients, 499.
Rathery, F., et Bordet, F., pulmonary gangrene cured by anti-gangrene serum, 316.
Ravaut, P., et Gallerand, leucoplacia treated by carbon dioxide snow, 114.
Ravina, A. : *see* Dufour, H., Semelaigne, G., et Ravina, A.
Rawlins, M., treatment of gonorrhoea in women, 215.
Ray, C. B. : *see* Shorten, J. A., and Ray, C. B.
Razzaboni, G., primary sarcoma of internal saphenous vein, 345.
Redlich, E., pathology of epilepsy following gunshot wounds of the skull, 448.
Reece, R. J., percentage of children vaccinated, 205.
Reenstierna, J., serum treatment of chancroid, 220.

Rehberg, mediastinal pleurisy, 318.
Rehfuss, M. E., and Hawk, P. B., gastric analysis. I. Fundamental principles. II. Interdigestive phase or principles governing phenomena of resting stomach, 474.
  hyperacidity, 4.
Rehn, E., ligation of internal carotid, 329.
Reiche, F., association of whooping-cough and influenza, 201.
  immunity against influenza, 304.
  jaundice in influenza, 299.
  mortality in whooping-cough, 201.
  urticaria tuberosa, 113.
  whooping-cough complicated with convulsions, 202.
Reichle, splanchnic anaesthesia, 524.
Reimer, G., caramel in treatment of diabetes, 506.
Reinhardt, A. : *see* Läwen, A., u. Reinhardt, A.
van der Reis, diagnosis of typhus by Friedberger–van der Reis, skin reaction, 197.
Reiss, J. : *see* Crohn, B. B., and Reiss, J.
Renaud, M., atypical primary epithelioma of lung, 317.
Renauld-Capart, H., cerebral metabolism. 3. Nature of substances secreted by liver which are essential for nervous centres, 476.
Renault, J., Schick test for susceptibility to diphtheria, 26.
Renaux, E., homogenization of tuberculous sputa and search for T.B. in cold abscesses, suppurative glands, and urines, 559.
Rénon, L., et Mignot, R., epidemiology of influenza, 295.
Rensch, O. B. : *see* Corper, H. J., and Rensch, O. B.
Rettger, L. F.: *see* Cheplin, H. A., and Rettger, L. F.
Rey, J. F., dysentery due to Morgan's No. 1 or No. 14 bacillus, 402.
Reyn, A.: *see* Chievitz, O., Jensen, J., Reyn, A., and Collin, E.
Ribadeau-Dumas, Mallet, et de Laulerie, radiological examination of kidneys after intraperitoneal insufflation, 286.
Ribierre, P., et Léobardy, J. de, gonococcal septicaemia, 211.
Richard, L., size of spleen in abdominal cancer, 120.
Richards, J. H., bacteriologic studies in chronic arthritis and chorea. Part I. Arthritis, 70.
Riche, general analgesia by intrathecal injections of novocaine, 523.
Richter, H., essential lesion of tabes, 547.
Richter, S., analysis of 601 cases of lumbar anaesthesia, 521.
Richter-Quittner, M.: *see* Falta, W., u. Richter-Quittner, M.
Rick, F., paravertebral injections in gynaecological cases, 523.
Riemschneider, G., diphtheritic paralysis of central origin, 24.
Rieux et Zoller, Shick test of susceptibility to diphtheria, 26.
Rist, E., et Strohl, A., experimental and critical studies on pneumothorax, 570.
Ritter, I. S. : *see* Stern, M., and Ritter, I. S.
Rivers, T. M., ligation of common carotid for haemorrhage into a post-scarlatinal abscess, 325.
Rivers, W. H. R., protopathic sensibility, 142.
  *see* Head, H., Rivers, W. H. R., and Sherren, J.
Rixon, C. H. L., and Matthew, D., anxiety hysteria, 349.
Roberts, D. : *see* Cole, L. G., and Roberts, D.
Robinson, G. H. : *see* Meader, P. D., and Robinson, G. H.
Robinson, G. H., and Meader, P. D., precipitin test for gonorrhoea, 213.
Rocci, X-ray therapy with new apparatus giving 200,000 volts, 287.
Rochaix : *see* Cluzet, Rochaix, et Kofman.
Rockwell, G. E., and McKhann, C. F., growth of gonococcus in various gaseous environments, 256.
Roederer, J.: *see* Adrian, C., et Roederer, J.
Roger, H., winter incidence of epidemic encephalitis and seasonal recurrence of chronic forms, 57.
Rohde, K., pancreatic necrosis, 510.
Rolf, I. P. : *see* Levene, P. A., and Rolf, I. P.
Rolleston, H., change of type in congenital syphilis, 410.
Rolleston, J. D., diphtheritic hemiplegia, 24.
Rolleston, J. D., and Macleod, C., intramuscular route for injection of diphtheria antitoxin, 28.
Rona, P., u. Petow, H., poisonous effect of thiodiglycol upon urease, 179.
Rosen, I. : *see* Fordyce, J. A., and Rosen, I.
Rosenbloom, J., occupation and bronchial asthma, 310.
Rosenmann, M., on fibrinolysis, 282.
Rösler, O. A., gastric ulcer due to plumbism, 5.
Ross, E. L., and Davis, L. H., difference between the mechanism of hyperglycaemia production by ether and by chloroform, 274.
Rosson, F. B. : *see* Du Bray, E. S., and Rosson, F. B.
Rothfeld, J., Freund, J., u. Hornowski, J., experimental investigations on pathogenesis and disseminated sclerosis, 347.
Rothlin, E., experimental studies of properties of surviving vessels under treatment with chemical stimuli, 378.
Roussy, G., thyroid lesions in Graves's disease, 247.
Routh, A., spirillolysis caused by chronic ferments, 407.
Roux : *see* Duval, P., Roux, et Béclère, H.
Rowland, C. C. : *see* Mackie, T. J., and Rowland, C. C.
Rowntree, L., Chesney, A. M., and Marshall, E. K., functional capacity of liver, 542.
Roy, M. P. L. J., radium treatment of cancer of cervix uteri, 584.
Rule, F. D. : *see* Peters, J. P., Barr, D. P., and Rule, F. D.

Rundle, G. W., results of antenatal treatment of syphilis, 413.
Rusca, C. L., Gaucher's disease, 170.
Russ, S., some problems in biological action of radiations, 185.
Russell, B. R. G., and Woglom, W. H., respiratory exchange of surviving mouse tissues, normal and neoplastic, 68.
Russell, T. H., abdominal symptoms in influenza simulating an acute surgical lesion, 300.
Rutherford, A. : *see* Cranston Low, R., Logan, W. R., and Rutherford, A.
Ruysch, W. P., typhus in Holland, 192.

v. Saar, G. F., u. Schamberger, R., treatment of acute suppuration of wrist, 236.
Sabouraud, R., alopecia areata an abortive form of congenital syphilis, 113.
Sachs, B., intraspinal treatment of neurosyphilis with salvarsanized serum, 338.
Sachs, E., and Malone, J. Y., alterations in brain volume of human subject by injections of hypertonic salt solutions, 536.
Salanier, M. : *see* Netter, A., et Salanier, M.
Salimbeni, d'Herelle's bacteriophage, 74.
Saloz, C. : *see* Cottin, E., Cramer, A., et Saloz, C.
Salvesen, H. : *see* Palmer, W. W., Salvesen, H., and Jackson, H.
Salvioli, G., histopathology of leprosy, 372.
Sampietro, G., sero-diagnostic studies on typhus, 170.
Sanborn, G. P., treatment of influenza by serum of convalescents, 305.
Sanfelice, F., changes shown by acid-resisting bacilli on passing through animal organism, 452.
Sänger u. Bornstein, electromyogram in amyotrophic lateral sclerosis, 533.
Sangiorgi, G. : *see* Fontana, A., e Sangiorgi, G.
Sappington, S. W., Gaucher's disease, 119.
Satani, Y., extra-mammary Paget's disease treated surgically, 114.
Sauer, L. W. : *see* Mattill, P. M., Mayer, K., and Sauer L. W.
Sauvé : *see* Chaton et Sauvé.
Savatard, L., early diagnosis of epithelioma of skin, 114.
  leiomyoma of smooth muscle-cells of arrectores pili, 114.
Saxl, P. : *see* Brunn, F., Hitzenberger, K., u. Saxl, P.
Saxtorph, S. M., influenza and tuberculosis, 302.
Schaefer, O. G. : *see* Dutiker, R. A., Eckles, C. H., Dahle, C. H., Mead, S. W., and Schaefer, O. G.
Schaeffer, F., and Chotzen, T., radiotherapy of tumours of hypophysis and of acromegaly, 582.
Schaffer, K., intramedullary bifurcation of posterior root fibres in man, 549.
  histopathology of tabes, 547.
Schamberger, R.: *see* v. Saar, G. F., u. Schamberger, R.
Schapiro, L., effects of treatment of ankylostomiasis in N. Queensland, 106.
Schaps, Th., danger of cocaine injections, 519.
Schemmel, E., treatment of injuries to vertebral artery, 332.
Schenk, P., action of histamin on man, 580.
  pituitary opotherapy of diabetes, 507.
Scheven : *see* Lehmann u. Scheven.
Schiassi, B., Graves's disease, 341.
Schick, B., breaking down of maternal blood as cause of icterus neonatorum, 580.
Schiffner, O. : *see* Jagic, N., u. Schiffner, O.
Schlagenhaufer, F., disappearance of vertebral bodies (osteolysis), 372.
Schlecht, deep radiotherapy in internal medicine, 487.
Schmerz, H., sacral anaesthesia, 525.
Schlomovitz, B. H., further experiments on effects of warming and cooling sino-auricular node in mammalian heart. Depth of anaesthesia, tachycardia, flutter, sino-auricular heart-block. (B) Experimental production of ventricular fibrillation by localized warming of cardiac tissue, 472.
Schmidt, V., sarcoma following radium treatment of epithelioma of tongue, 583.
  100 cases of paralysis of recurrent laryngeal nerve, 254.
Schmidtmann, M. : *see* Brahn, B., u. Schmidtmann, M.
Schmieden, V., kinking of bile-duct, 128.
Schmiegelow, E., fatal haemorrhage following removal of adenoids, 328.
Schmiesing, T., digestion of infants' foods, 387.
Schmilinsky, gastric operations under splanchnic anaesthesia, 524.
Schnabel, A. : *see* Doerr, R., Schnabel, A., u. Vöchting, K.
Schneider, E. C., and Truesdell, D., study of low oxygen effects during rebreathing, 382.
Schoemaker, J., pericolitis membranacea, 226.
Schönfelder, T., diphtheria of umbilicus, 20.
Schou, H. J., nerve lesions in early syphilis and their treatment, 61.
Schultz, O. T. : *see* Anderson, R. A., and Schultz, O. T.
Schulz, W., course of creatinin excretion in urine in man, with especial reference to effect of exercise, 180.
Schütze, H., haemagglutination and its medico-legal bearing, with observations upon the theory of isoagglutinins, 163.
Schwalbach, G., aneurysm of vertebral artery, 333.
Schwarz, H. : *see* Wessler, H., and Schwarz, H.
Schweinburg, E., epidemic of typhus among German prisoners in Orenburg (Russia) in 1915, 193.
Scott, E. L., sugar in blood of dog-fish and sand-shark, 471.
Scott, E. L., and Honeywell, H. E., study of sugar in blood of normal pigeons, 472.
Scott, E. L., and Kleitmann, N., sugar in blood of common frog, 471.

Scruton, W. A., hemiplegia occurring immediately after tonsillectomy, 327.
Sebilleau, P., death caused by removal of tonsils, 327.
Seelig, M. G., cholecystectomy, 129.
Segagni, S., pseudo-ascites in children, 13.
Séguin, P., beneficial effect of certain bacteria in cultivation of buccal spirochaetes, 270.
Semelaigne, G. : *see* Dufour, H., Semelaigne, G., et Ravina. A.
Sencert, L. : *see* Nageotte, J., et Sencert, L.
Senevet, G. : *see* Lapin, J., et Senevet, G.
Sessa, P., study of gall-stones by X-rays, 92.
Sevestre : *see* Houzel et Sevestre.
Seyfarth, C., arteriovenous aneurysm between carotid artery and cavernous sinus, 425.
Sharp, W. B. : *see* Jordan, E. O., and Sharp, W. B.
Shattock, S. G. : *see* Nitch, C. A. R., and Shattock, S. G.
Shaw, W. F., and Burrows, A., Wertheim's hysterectomy for advanced carcinoma of cervix made possible by use of radium, 584.
Shearer, C., amount of heat liberated by *Bacillus coli* when grown in presence of free amino-acids, 567.
Shellshear, J. L., basal arteries of forebrain, and their functional significance, 348.
Sherren, J. : *see* Head, H., Rivers, W. H. R., and Sherren, J.
Sherrill, J. W. : *see* Allen, F. M., Mitchell, J. W., and Sherrill, J. W.
Sherrington, C. S., integrative action of nervous system, 145.
  nature of tonic contraction of muscle, 532.
  scratch reflex in spinal cat, 429.
Shipley, P. G. : *see* McCollum, E. V., Parsons, H. T., Shipley, P. G., and Park, E. A.
von Sholly, A. I., and Park, W. H., report on prophylactic vaccination of 1,536 persons against acute respiratory diseases, 1919–20, 267.
Shorten, J. A., and Ray, C. B., antiscorbutic and anti-beri-beri properties of certain sun-dried vegetables, 574.
Sicard, J. : *see* Bonnet, E., et Sicard, J.
Simmonds, N. : *see* McCollum, E. V., Simmonds, N., Parsons, H. T., Shipley, P. G., and Park, E. A.
Simmons, J. S., diphtheria caught from cat, 18.
Simmons, J. S., Wearn, J. T., and Williams, O. B., diphtheria infections with particular reference to carriers and to wound infections with *B. diphtheriae*, 454.
Singer, G., gastro-intestinal haemorrhage in polycythaemia hypertonica and syphilitic aortitis, 11.
Sippel, P., congenital torticollis, 132.
Skajaa, K., pathological-anatomical and bacteriological study of influenza and influenzal pneumonia, 562.
Skramlik, E. : *see* Hahn, M., u. Skramlik, E.
Slemons, J. M., analysis of blood in eclampsia, 538, 540.
Sloboziano : *see* Constantinesco, C. D., et Sloboziano.
van Slyke, D. D., carbon dioxide carriers of the blood, 379.
  *see* Palmer, W., and van Slyke, D.
  *see* Losee, J. R., and van Slyke, D.
Smillie, W. G., beta naphthol in treatment of hookworm infection, 107.
Smith, C. A. : *see* Hawk, P. B , Smith, C. A., and Bergeim, O.
Smith, E. B., splenectomy for splenomegalic cirrhosis, 124.
Smith, J. D., and Wilson, M. A., comparison of smear, culture and complement fixation in chronic gonorrhoea in women, 157.
Smith, J. W., results of operations for atony and prolapse of large intestine, 223.
Snell, M., umbilical diphtheria, 22.
von Sohlern, gastro-intestinal haemorrhage, 11.
Sörensen, microscopic examination of organs from cases of influenza, 264.
Sorrel, Étienne, infantile deforming osteochondritis of upper epiphysis of femur, 39.
Soucek, A., vaccination in Bavaria, 205.
Speed, K., carcinoma of pancreas, 512.
Spencer, W. G., arterial haemorrhage from ear and its control by ligature of common carotid, 326.
  injury to vertebral artery, 332.
Spencer, W. G., and Horsley, V., connexions of internal carotid in monkeys, 323.
Spencer, W. G., and Keith, A., melanin chromatophores in submucous tissue of caecum and colon, 228.
Spiethoff, B., sources of error in treatment by salvarsan, 158.
Spiller, W. G., treatment of spastic gait by permanent flexion of great toe, 548.
Spolverini, L., vaccine treatment of whooping-cough, 204.
Spriggs, E. I., duodenal diverticula, 183.
Stark, H. S., obesity and diabetes, 504.
Starling, E. H. : *see* Kaya, A., and Starling, E. H.
Starlinger, rate of sedimentation of red cells during pregnancy, 543.
Stearns, G., and Lewis, H. B., diet and sex as factors in creatinuria of man, 469.
Steenbock, H. : *see* Hart, E. B., Steenbock, H., and Ellis, N. R.
Steffen, G. I. : *see* Cecil, R. L., and Steffen, G. I.
Stein, R. O., differential diagnosis between large- and small-spored ringworm, 112.
Stengel, A., association of glycosuria with infectious diseases, 497.
Stephenson, M., differentiation of yellow plant pigments from fat-soluble vitamine, 84.
Stepp, W., and Feulgen, R., identification of aldehyde-like substance in diabetic urine as acetaldehyde, 576.
Stern, A., herpes febrilis, 112.
Stern, M., and Ritter, I. S., intravenous injections of sodium iodide in treatment of

gonorrhoeal arthritis, epididymitis, and prostatitis, 214.

Stertz, G., organization of extrapyramidal motor system and selective incidence of paralyses of pyramidal origin, 443.

Stettner, E. : *see* Jamin, F., u. Stettner, E.

Stevens, W. E., and Heppner, M., occurrence and treatment of chronic gonorrhoea in women, 214.

Stevenson, G. S. : *see* Ebaugh, F. G., and Stevenson, G. S.

Stewart, G. N., and Rogoff, J. M., post-operative depletion and epinephrin store of adrenals, 476.

Stillman, E. G., and Bourn, J. M., biological study of haemophilic bacilli, 154.

Stoichitia, I., blood in influenza, 297.

Stokes, A., and Bigger, J. W., dysentery epidemic in Dublin, 1919, 399.

Stolkind, E. J., congenital syphilitic aortitis, 410.

Storm van Leeuwen, W., and Zeijdner, J., influence of colloids on action of non-colloidal drugs, 282.

Stoyanovitch, M. D., gas cysts of intestine, 11.

Strandberg, J., et Hedenius, J., chronic gonorrhoeal arthritis complicated by keratodermia blenorrhagica. 212.

Strassberg, M., influenza in syphilitic women, 303.

Straub, H., u. Meier, K., blood gas studies. VIII. Influence of certain digitalis bodies on permeability to ions of human red blood corpuscles, 174.

Strauss, E., composition of keratin, 110.

Strauss, H., diagnosis of duodenal ulcer, 6.

Strauss, O., radiotherapy and polycythaemia, 390.

Strauss, R., gastric cancer, 7.

Strickler, A., and Goldberg, J. M., anaphylactic food reactions and eczema, 110.

Stroë, A., cerebrospinal fluid in typhus, 195.

Strohl, A. : *see* Rist, E., et Strohl, A.

Strominger, L., cystitis after typhus, 196.

Strouse, S., renal glycosuria, 503.

Sturm, E. : *see* Murphy, J. B., Nakahara, W., Sturm, E.
  *see* Murphy, J. B., Nakahara, W., Hussey, R. G., Sturm, E.

Suitsu, N., alkaline reserve of blood of insane, 277.

Sullivan, M., and Dawson, P. R., sulphocyanate content of saliva and urine in pellagra, 283.

Sundstroem, E. S., and Bloor, W. R., physiological effects of short exposures to low pressure, 174.

Sundt, H., malum coxae Calvé-Legg-Perthes, 39.

Sutherland, G. F., gastric secretions in starvation, 473.
  response of stomach glands to gastrin before and shortly after birth, 474.

Swanbeck, C. E. : *see* Karsner, H. T., and Swanbeck, C. E.

Symes, J. O., pancreatic calculi, 513.

Tallo, F., action *in vitro* of neosalvarsan on *B. anthracis* from cultures (without capsule) and from the animal organism (with capsule), 458.

Taniguchi, T., Sachs-Georgi syphilis reaction and its relation to Wassermann reaction, 362.

Taylor, J., colectomy, 223.

Taylor-Jones, E., action of induction coils, 181.

Teague, O., and Deibert, O., diagnosis of chancroid, 219.

Ten Horn, plication of caecum in treatment of constipation, 227.

Tewksbury, W. D., pulmonary abscess, 314, 315.

Thewlis, M. W., gargling with chloral hydrate solution in treatment of influenza, 305.
  influenza in old age, 303.

Thibierge, G., lichen planus distinct from lichen simplex, 111.

Thjøtta, Th., studies on bacterial nutrition. I. Growth of *Bacillus influenzae*, in haemoglobin-free media, 562.

Thjøtta, T., and Avery, O. T., growth accessory substances in nutrition of bacteria, 387.

Thomsen, O., and Christensen, S., types of pneumococci, 73.

Thomsen, O., and Vollmond, E., an attempt to classify gonococci according to type, 157.

Thomsen, O., u. Wulff, F., certain problems concerning meningococcal infection, 258.
  experimental studies of mode of action of antimeningococcal serum, 63.

Thormälen, J., melanogen in urine of woman suffering from melanotic cancer, 229.

Tibaldi, E., on a new species of parasitic amoeba occurring in crypts of tonsils (*Entamoeba macrohyalina*), 457.

Tichy, H., results of treatment of cancer of breast by excision and radiation, 421.

Tisdall, F. F., estimation of phenolic substances in urine, 86.

Tocunaga, H., biology of influenza bacillus, 58.

Tomkinson, J. G., X-rays in treatment of oriental sore, 114.

Tonnet, J.: *see* Loeper, M., Forestier, J., et Tonnet, J.

Torraca, L., lesions of nerve-cells of parietal plexuses of gastro-enteric canal in consequence of surgical interventions, 371.

Torraca, T., on epithelioma adenoides cysticum (Brooke) or tricho-epithelioma papillosum multiplex (Jarisch), 464.

Trask, J. D. : *see* Blake, F. G., and Trask, J. D.

Trendelenburg, P., u. Groebel, W., relation between parathyroid tetany and calcium deficit in blood, 278.

Trenkel, H., value of Wildbolz's auto-urine reaction in demonstration of active tuberculosis, 559.

Treupel, G., chronic lung disease following influenza, 297.

Treupel u. Kayser-Petersen, immunity against influenza, 304.
Tröndle, A., new experiments on uptake of substances by cell, 478.
Trotter, W., on certain clinically obscure malignant tumours of nasopharyngeal wall, 242.
  pathological physiology of the skull, 428.
Trotter, W., and Morriston Davies, H., results of experimental nerve section in man, 46.
Truesdell, D.: *see* Schneider, E. C., and Truesdell, D.
Tuffier, cancer of oesophagus treated by direct application of tube of radium emanation to oesophageal wall through transpleural channel, 284.
Tuohy, E. L., splenomegaly with polymorphonuclear neutrophil hyperleucocytosis, 121.
Turnbull, H. M., glycogenic infiltration of liver of laboratory rabbits, 67.
Turner, C. G., discoloration of abdominal wall as sign of acute pancreatitis, 514.
Turretini, G., et Gerber, I., gastric cancer, 8.
Twort, F. W., researches on dysentery, 57.

Udaondo, C. B., y Carulla, J. E., syphilis of pancreas, 512.
Uhlenhuth, E., experimental production of gigantism by feeding anterior lobe of hypophysis and pituitary gland, 179.
v. Uji, S., intestinal obstruction caused by ascarides, 104.
Umber, F., diabetes and pregnancy, 501.
Unger, L. J.: *see* Hess, A. F., and Unger, L. J.
Unneberg, A.: *see* Williams, A. W., Unneberg, A., Goldman, A., and Hussey, H.
Urbantschitsch, E., case of influenza with bilateral choked disc and unilateral paralysis of 6th nerve, 300.

Vaccarezza, R. F., y Finochietto, R., case of acute amoebic dysentery, 402.
Vallardi, C., epidemiological and clinical notes on protozoan dysentery, 456.
  dysentery epidemic in Macedonia, 1918, 399, 456.
  mixed dysenteric forms, 456.
  sero-diagnosis in bacillary dysenteric infections, 456.
Vandenbosche, instant death during removal of tonsils, 327.
Váró, B., effect of the war on incidence and mortality of eclampsia, 542.
Vaudremer, hypopyon complicating typhus, 196.
  treatment of typhus, 198.
Vaudremer, A., facultative acid fastness in tubercle bacilli, human and bovine, 260.
Vaurs, R., perforation of stomach in gastric cancer, 8.
Vernon, H. M., apnoea after forced respiration, 432.
Viannay, C., injury causing spasmodic contraction of arteries, 33, 34.
Vicente, M., bile enemata in treatment of constipation, 15.
  *see* Bensaude, R., et Vicente, M.
Viets, H., relation of form of knee-jerk and patellar clonus to muscle tonus, 54.
Vigevani, G., pituitary opotherapy of diabetes, 507.
Vigne, P.: *see* Civatte, A., et Vigne, P.
Vines, H. W. C., rôle of calcium in coagulation of blood, 558.
Vochting, K.: *see* Doerr, R., Schnabel, A., u. Vöchting, K.
Vogel, C., tuberculosis cutis vegetans, 112.
Vogt, H., dysentery in children during epidemic at Barmen, 1899-1901, 400.
Vollmond, E.: *see* Thomsen, O., and Vollmond, E.
Volpino, G., e Desderi, P., microscopic observations on brains from some cases of epidemic encephalitis, 452.
Vorschütz, J., investigation on agglutination and sedimentation of bacteria, 176.

Wagener, H. P., and Wilder, R. M., retinitis in diabetics, 499.
Wagner, K., complications of vaccination, 208.
Waite, J. H., and Neilson, I. L., ankylostomiasis in N. Queensland, 106.
Walker, I. C., hay fever, 309.
  fibrinous bronchitis, 312.
Wallgren, A., acute leukaemia in pregnancy: an argument against theory of infectious origin of disease, 64.
Wallis, R. L. M., tests for functional activity of pancreas, 514.
Walshe, F. M. R., conditions of extensor muscles in spastic paralysis, 533.
  relationship between muscle tone and tendon reflexes, 532.
Walterhofer, G., action of X-rays in leukaemia, 486.
Warburg, O., u. Negelein, E., oxidation of cystin and other amino-acids by blood charcoal, 480.
Ward, E., urticaria following acute fevers, 113.
Wassermann, S., skin pigmentation in soldiers, 112.
Watson, A.: *see* Paton, D. N., and Watson, A., 574.
Waugh, G. E., surgical treatment of mobile caecum and ascending colon, 227.
Wearn, J. T.: *see* Simmons, J. S., Wearn, J. T., and Williams, O. B.
Webster, L. T.: *see* Lewis, W. H., and Webster, L. T.
Weed, L., and McKibben, P., experimental production of alterations in cerebrospinal fluid pressure and brain volume, 535.
Weichbrodt, R., intraspinal treatment of neurosyphilis, 339.
Weil, M. P., cystic pneumatosis of intestine, 11.
Weil, P. E., Wassermann reaction in chronic splenomegaly, 121.

Weil, P. E., et Plichet, diabetes and hirsuties, 502.
Weill, E., et Dufourt, A., intramuscular injection of ether in treatment of whooping-cough, 202.
Weill-Hallé, B., intramuscular route for injection of diphtheria antitoxin, 28.
Weinberg, J. A., influence of exposure to X-rays on growth of tuberculosis, 395.
Weinberg, M., et Kepinow, L., leuco-agglutinins, 461.
Weinberg, M., et Otelesco, I., *B. proteus* of war wounds, 451.
Weiss, H., heat resistance of spores, with special reference to spores of *B. botulinus*, 352.
Weiss, M., analysis of colouring substances of urine. II. Urochromogen, 282.
Weiss, W., salvarsan in treatment of pulmonary gangrene, 316.
Wertheim Salomonson, J. K. A., electromyogram in tendon reflexes, 531.
  electromyogram in nervous diseases, 533.
Wessler, H., pulmonary abscess, 314.
Wessler, H., and Schwarz, H., pulmonary abscess, 315.
Westergren, A., suspension stability of blood in pulmonary tuberculosis, 366.
Westphal, A., unusual motor symptoms in disseminated sclerosis, with reference to differential diagnosis from epidemic encephalitis, 248.
White, C., sodium bicarbonate tolerance in normal and toxaemic pregnancies, 539.
White, C. J., anaphylactic food reactions and eczema, 111.
White, H. L., and Erlanger, J., effect on composition of blood of maintaining an increased blood-volume by intravenous injection of gum acacia in normal, asphyxiated, and shocked dogs, 273.
Widal, F., et May, E., gonococcal septicaemia complicated with icterus, 211.
Widal, F., Abrami, P., et Iancoresco, N., effect of glucose on white blood count of diabetics, 498.
Wiener, H. J.: *see* Mosenthal, H. O., and Wiener, H. J.
Wieting, wound diphtheria, 23.
Wilder, R. M.: *see* Wagener, H. P., and Wilder, R. M.
Wildhagen, K., primary round-celled sarcoma of lung, 317.
Wile, U. J., syphilis of pancreas, 511.
Williams, A. W.: *see* Park, W. H., Williams, A. W., and Krumwiede, C.
Williams, A. W., Nevin, M., Gurley, C. R., methods of demonstrating micro-organisms including 'filtrable viruses' from upper respiratory tract in 'health' in 'common colds', and in 'influenza', with the object of discovering 'common strains', 267.
Williams, A. W., Unneberg, A., Goldman, A., and Hussey, H., relationship to upper respiratory infections of streptococci producing a green zone on standard blood-agar plates (Smith and Brown's alpha type), 267.
Williams, J. W., causation of foetal deaths, 407.
  value of Wassermann reaction in pregnancy, 409.
Williams, O. B.: *see* Simmons, J. S., Wearn, J. T., and Williams, O. B.
Williamson, R. T., dietetic treatment of diabetes, 505.
van der Willigen, A. M. M., purgative action of sulphur—of calomel—of phenolphthalein, 180.
Wilson, C. M.: *see* Pannett, C. A., and Wilson, C. M.
Wilson, D. W., pyrimidine metabolism, 89.
Wilson, G. H.: *see* Browning, C. H., and Wilson, G. H.
Wilson, M. A.: *see* Smith, J. D., and Wilson, M. A.
Wilson, S. A. K., on decerebrate rigidity in man and occurrence of tonic fits, 55.
Wishart, M. B., experiments on carbohydrate metabolism and diabetes. III. Permeability of blood corpuscles to sugar, 86.
  *see* Allen, F. M., and Wishart, M. B.
Wishart, M. B., and Pritchett, I. W., experimental studies in diabetes: gas bacillus infections in diabetic dogs, 273, 275.
With, C., effects of light baths on vitiligo, 111.
De Witt, L. M., mercury compounds in chemotherapy of experimental tuberculosis in guinea-pigs, 262.
  weight curves of tuberculous guinea-pigs, 82.
Witzemann, E. J., disodiumphosphate as a catalyst for quantitative oxidation of glucose to carbon dioxide with hydrogen peroxide, 178.
Woglom, W. H.: *see* Russell, B. R. G., and Woglom, W. H.
Wolf, C. G. L., influence of reaction of media and of presence of buffer salts on metabolism of bacteria, 66.
  *see* Ewing, J., and Wolf, C. G. L.
Wolff, E.: *see* Neuberg, C., Nord, F. F., u. Wolff, E.
Wollman, E., d'Herelle's phenomenon, transmissible microbic autolysis of Bordet and Ciuca, and Darwin's theory of pangenesis, 74.
Woloshin, B., treatment of bronchial asthma by hypodermic injection of benzyl benzoate, 312.
Wood, F. M., treatment of diphtheria by injecting devitalized Klebs-Loeffler bacilli and antitoxin, 30.
Woodman, H. E., comparative investigation of corresponding proteins of cow and ox serum, cow's colostrum and cow's milk by method of protein racemization, 575.
Wörner, E.: *see* Moog, O., u. Wörner, E.
Wright, A. E., 'intertraction' between albuminous substances and saline solutions, 577.
Wu, H.: *see* Aub, J. C., Cunningham, T. D., and Wu, H.
Wulff, F.: *see* Thomsen, O., u. Wulff, F.

Wulff, P., aneurysm of internal carotid after tonsillar abscess, 325.

Wuth, G., biological effect of proteinogenous amines. A contribution to question of acetonitrile reaction, 578.

Yamane, Jinshin, physical and chemical properties of horse semen in relation to physiology of spermatozoa, 477.

Young, J., and Miller, D. A., eclampsia due to absorption of toxic products from degenerated portions of placenta, 544.

Young, M. L., amoebic dysentery in London Children's Hospital, 400.

Zanelli, P., action of continuous electric current on agglutinating sera, 355.

Zappa, P., on normal leucocytic formula, 169.

Zeijdner, J. : *see* Storm van Leeuwen, W., and Zeijdner, J.

Zeller, H. : *see* Herzog, F., u. Zeller, H.

Zenoni, C., e Macchi, A., pulmonary streptothricosis, 316.

Zielinski, C., treatment of typhus by intravenous injection of patient's cerebrospinal fluid, 198.

Zilva, S. S., action of ozone on fat-soluble factor in fats, 85.

*see* Drummond, J. C., Golding, J., Zilva, S. S., and Coward, K. H.

Zlocisti, T., typhus in German Red Cross Hospital at Constantinople, 193.

Zoeller : *see* De Lavergne et Zoeller.

Zoepffel, H. : *see* Neumann, J., u. Zoepffel, H.

Zondek, S. G., importance of colloidal nutrient solutions for normal, exhausted, and poisoned heart, 576.

Zweifel, E., sacral anaesthesia, deaths from, 525.

theories as to cause of eclampsia, 537, 544.

Zoller : *see* Rieux et Zoller.

PRINTED AT OXFORD, ENGLAND
BY FREDERICK HALL
PRINTER TO THE UNIVERSITY

# MEDICAL SCIENCE

## ABSTRACTS & REVIEWS

VOLUME IV. NUMBER 1 APRIL 1921

## CONTENTS

REVIEWS: PAGE

ALIMENTARY DISEASES . . . . . . . . . . . . . . 3

DIPHTHERIA . . . . . . . . . . . . . . . . 18

INJURY CAUSING SPASMODIC CONTRACTION OF SEGMENTS OF ARTERIES OF MEDIUM SIZE . . . . . . . . . . . . 33

NON-TUBERCULOUS JUVENILE COXALGIA . . . . . . . . 38

ANTERIOR DISLOCATION AT THE ELBOW . . . . . . . . 41

THE PHYSIOLOGY OF PAIN . . . . . . . . . . 43

ABSTRACTS:

SURGERY . . . . . . . . . . . . . . . . . 52

NEUROLOGY . . . . . . . . . . . . . . . . 53

PATHOLOGY AND BACTERIOLOGY . . . . . . . . . . 57

BIOCHEMISTRY . . . . . . . . . . . . . . . 84

RADIOLOGY AND ELECTROLOGY . . . . . . . . . . 91

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# REVIEWS

## ALIMENTARY DISEASES

Jardet records four cases of **parotid swelling** occurring in adults characterized by sudden enlargement of the gland, which almost always occurred after the first meal of the day and rapidly increased during mastication, its subsequent development depending on whether it was a primary attack or a relapse, and the character of the food. The swelling was accompanied by local tension, restricted movement of the jaw, and sometimes by pain, which was acute for the first half hour and dull afterwards, as in mumps. Contrary to what occurs in mumps, however, on pressure on the gland distinct lobulation could be felt, and occasionally a hard cord of the size of a pencil representing Steno's duct. Pressure on the gland caused expulsion of a plug of mucus followed by a flow of saliva. The affection usually starts the first week that a tooth-plate is worn, but it may occur later. It may last for some days, but usually disappears more or less completely the same day, and recurs the next and for five or six days in succession. It then subsides, but returns after an interval of a month or six weeks as the result of a chill, irritating food, or the onset of menstruation. The condition is due to the tooth-plate producing irritation of the gum and obstruction of the orifice of Steno's duct with subsequent retention of saliva. Cure is effected by removal of the tooth-plate and its careful readjustment, together with the use of a potassium chlorate mouth-wash.

**Gastric analysis.** Brüning, director of the Rostock University Children's Clinic, reports the results of about 300 examinations of the gastric contents in children aged from 2 to 15 years. While the total normal acidity in adults is 30–60 and the average free hydrochloric acid is 20–40, the average total acidity in children was found to be 48·8 and the free hydrochloric acid 14·3. Hardly any differences were noted between boys and girls, either in the upper or lower classes of society. On the other hand the figures rose as the age of the child advanced. Thus between 2 and 10 years the total acidity was 46·9 and the free hydrochloric acid 11·5, and between 11 and 15 the total acidity was 52·8 and the free hydrochloric acid 20·1. During the war there was almost invariably a diminution of the hydrochloric acid values, as was found by other writers in adults. On ranging the children in two groups, according as their digestion was normal or diseased, it was found that the total acidity and free hydrochloric acid were higher in normal children than in those suffering from gastro-intestinal disturbance. There were no less than 63 cases, or 21 per cent., with hypochlorhydria or achlorhydria. It was a remarkable fact that 13 of the cases of achlorhydria had no gastro-intestinal symptoms, while the rest suffered from abdominal pain, diarrhoea, or constipation.

As the result of a study of a large number of cases, Rehfuss and Hawk found that the normal individual elaborates acid figures as high as those commonly associated with pathological conditions, no acid figures being found in disease which exceeded the figures present under certain circumstances in health. The average acid finding during the digestion of certain foods in the normal stomach was found to be within the range which is accepted by all clinicians as abnormal. It was found that approximately 40 per cent. of normal individuals constantly show the acid titration findings of so-called hyperacidity.

Dupuy describes the test of sham feeding introduced by Carnot in 1904 as the practical application of Pavlov's well-known experiments. After preliminary catheterization of the stomach before breakfast to determine if there is any stasis, in which case the stomach is completely emptied, the patient is given an appetizing meal of ten minutes' duration, which he is told to masticate slowly without swallowing, the food and saliva being spat out after mastication into a special basin. He is then left for ten minutes, and told not to swallow but to spit out the saliva secreted. At the end of this time the catheter is passed again, and in normal cases 60–90 c.c. of clear fluid is withdrawn without any particles of food. The free hydrochloric acid varies from 1·64 to 1·80 and the total acid from 1·80 to 1·96. In seven out of eight cases of cancer of the stomach Dupuy found that the total acid was below 1 and that there was an absence of free hydrochloric acid. In gastric ulcer the quantity of gastric juice secreted after sham feeding was normal in the case of ulceration of the body of the stomach, and generally increased in active or recently healed prepyloric or pyloric ulcer. In duodenal ulcer the secretion was usually increased. In dyspepsia due to gall-stones there was an excess of secretion and of hydrochloric acid. In nervous dyspepsia the secretion might be normal, exaggerated, or defective in amount and acidity. In tabes the secretion was often entirely absent.

In alcoholism hyperchlorhydria was usually present in the early stage, but later the amount of hydrochloric acid diminished, falling in extreme cases as low as 0·365. In tuberculosis with anorexia the quantity of gastric juice withdrawn after sham feeding was normal, but the fermentative activity of the gastric juice was still more diminished than its acidity. Dupuy concludes by saying that 'sham feeding' should be adopted as a routine method in the examination of gastric chemistry.

Carnot describes the following three forms of **plastic linitis** according as the process affects the body of the stomach only or involves the orifices as well: (1) gastric linitis without involvement of the orifices; (2) cardio-gastric linitis; (3) gastro-pyloric linitis. The characteristic features of the first form are microgastria, rigidity, and thickening of the wall of the stomach. The symptoms are dysphagia and regurgitation resulting from the small capacity of the stomach. In cardio-gastric linitis there is a rigidity of the cardiac orifice which is manifested by stenosis of the cardiac end of the stomach. The symptoms consist in dysphagia and regurgitation of mucus and food. The oesophageal bougie is arrested at the cardiac orifice or even higher up, at least 40 cm. from the teeth. Diagnosis of a new growth at the cardiac end of the stomach in such cases is therefore almost inevitable. In gastro-pyloric linitis there is a rigidity of the pyloric orifice, giving rise to pyloric incontinence which predominates over pyloric stenosis.

**Gastric and duodenal ulcer.** In discussing the aetiology of gastric and duodenal ulcer, Hurst states that he has seen a number of cases in which two or more brothers and sisters have suffered from gastric and duodenal ulcers, and still more in which brothers and sisters of a patient with a gastric or duodenal ulcer have had symptoms of a similar character, but so much less severe that it seemed impossible that actual ulceration was present. In one family the father and two out of nine children were dyspeptic and four others had typical symptoms of duodenal ulcer, one dying from a perforation. Hurst has never seen one member of a family with a gastric ulcer and another with duodenal ulcer. This suggests that the types of stomach which predispose to the development of gastric and duodenal ulcer respectively are congenital, and either one or the other may exist in several members of a family.

Albu also considers that a congenital predisposition to peptic ulcer exists, and remarks that all experienced practitioners have known families in which a so-called 'weak stomach' is transmitted from one generation to another. This condition is often nothing but a latent gastric or duodenal ulcer. In the pathogenesis of gastric and duodenal ulcer he distinguishes a series of different factors which include a predominant nervous or vagotonic cause, insufficiency of the organs, and various occasional causes.

According to Boas of Berlin, the frequency and severity of chronic gastric ulcer have recently shown a decided increase, which is manifested by the frequency of haematemesis, relapses, and perforation. It is natural to suppose that war diet is chiefly responsible for these complications, but Boas draws attention to another factor which has not received sufficient attention, namely, an increased amount of heavy work, particularly in women living in the country, who in the absence of their husbands on military service had to undertake work which was out of proportion to their strength.

Nicolaysen reports ten cases of haemorrhagic erosions of the stomach or duodenum observed in the course of the last two years at the Rikshospital, Christiania. In six of the cases irritation of the vagus was produced during the course of the illness, which in every case was situated in the brain or its membranes. In a second group of three cases the disease involved the chest, the lungs and pleura being the seat of infiltrating processes. In the last case, one of peritonitis with empyema, there may have been involvement of the nerves of the stomach in the abdomen as well as in the thorax. Nicolaysen's results show that in most of the cases in which haemorrhagic erosions were found there had been irritation of the vagus or the possibility of such irritation.

Rösler, of the Graz University Medical Clinic alludes to Schiff's recent article on the relation of gastric ulcer to plumbism (vide *Medical Science*, 1920, **1**, 584–5) and records a case in which a gastric ulcer developed as a sequel of a functional spastic hour-glass contraction in a woman aged 25, the subject of chronic plumbism.

The occurrence of ascites in connexion with duodenal ulcer is an extremely rare event. Only one example of the kind occurred among 129 cases of duodenal ulcer operated on by Haberer, a little free fluid being evacuated on laparotomy. Out of 121 cases of duodenal ulcer operated on by Finsterer, from whose paper this information is taken, in only two was there a large amount of ascites present. In one of them, however, there was hepatic cirrhosis, while in the other the liver was quite normal, but the ascites was due to compression of the portal vein. Complete recovery followed excision of the ulcer. The fact that duodenal ulcer may give rise to considerable ascites is of diagnostic and prognostic importance, because exploratory laparotomy which might reveal the true condition might be declined on the mistaken idea that malignant degeneration of the ulcer was responsible for the ascites.

Brunn, Hitzenberger, and Saxl, recently examined 69 cases of gastric or duodenal ulcer which had been treated at the First Medical Clinic in Vienna between 1911 and 1919, and found that in both gastric and duodenal ulcer there is a period of complete absence of symptoms which alternates with a period in which symptoms are present. Even in this latent period objective signs, and especially X-ray changes, can be detected. The writers therefore conclude that only a very small number of cases of gastric or duodenal ulcer can be regarded as cured.

The value of the string test in the diagnosis of peptic ulcers and their location is illustrated by Einhorn (1). The test is performed as follows: The duodenal bucket, attached to a thread, a knot in which is made at the teeth, is swallowed in the evening after supper with a glass of water. In the morning before breakfast it is slowly withdrawn and the thread is examined for blood spots and bile stains. The distance of the blood spots from the knot at the teeth will show the location of the ulcer. Thus a bloodstain at about 40 cm. (16 in.) points to an ulcer of the cardia; from 44–54 cm. ($17\frac{1}{2}$–$21\frac{1}{2}$ in.), ulcer of the lesser curvature; from 55–56 cm. (22–$22\frac{1}{3}$ in.), ulcer of the pylorus; 57 cm. ($22\frac{1}{2}$ in.) and more, duodenal ulcer. Einhorn regards the thread test as of importance not only in the recognition of the position of the ulcers, but also as a criterion of the efficiency of treatment, especially in determining whether a cure has been effected or not.

According to H. Strauss, of Berlin, apart from certain rare X-ray findings, there is no single symptom really pathognomonic of duodenal ulcer. Since 1911 he has maintained that for practical purposes it is sufficient to make a diagnosis of parapyloric ulcer, a term which includes all ulcers on either side of the pylorus as well as in the pylorus itself, and that a diagnosis of this condition is more frequently correct than the difficult one of duodenal ulcer. He regards the triad of symptoms—hyperaesthesia, hypersecretion, and hypermotility as to a certain extent characteristic of the parapyloric symptom-complex. He considers hypersecretion as more important than hyperacidity. In his experience two-thirds to three-quarters of all cases of hypersecretion are due to a parapyloric affection. He points out that manifest or occult haemorrhages are by no means a necessary symptom of ulcer, the number of negative blood findings in the faeces varying with different writers from 25 to 50 per cent. On the other hand, he regards the undoubted presence of blood in the faeces as of very great diagnostic significance.

Dunham maintains that visceral syphilis is frequently responsible for errors in the diagnosis of duodenal ulcer, and for the last five years has had a routine Wassermann reaction made on every patient with chronic digestive disturbance. If signs of syphilis are found after making a diagnosis of duodenal ulcer, the patient should be given thorough antisyphilitic treatment, even if the Wassermann reaction is negative.

According to Ramond, **pyloric spasm** is a very frequent affection, but its symptoms, which are usually attenuated, readily escape notice. In some cases, however, they are very pronounced. The causes of pyloric spasm may be local, reflex, or general. The local causes, which are the most numerous and important, include gastritis, gastric ptosis, and badly masticated food. Reflex pyloric spasm is most frequently due to cholelithiasis and appendicitis, less frequently to renal calculus, pancreatic lithiasis, floating kidney, and constipation. General causes consist of intoxications, especially tobacco, and emotions. Two forms of pyloric spasm may be distinguished, viz. an intermittent form, which is much the commonest, and a continuous type. In the intermittent type the spasm may occur at the beginning of digestion or later. The patient has a sudden loss of appetite, and gaseous eructations occur with or without pyrosis and regurgitation of food. Nausea and vomiting are exceptional. In a few moments the spasm ceases and there is almost immediate relief. Continuous pyloric spasm, of which Ramond and Clément report an example, is manifested by continuity of all the above symptoms, the condition in course of time closely resembling pure pyloric stenosis with dilatation.

Lichtenstein has come to some unorthodox conclusions concerning pylorospasm, 24 cases of which were treated at the Sachska Children's Hospital. These cases represent 1·9 per cent. of all the patients under one year. There were only 5 females to 19 males. and the numbers of breast-fed and artificially fed infants were approximately equal. It was noted that, even in severe and perfectly typical cases, the pylorus might never be palpable. A palpable pylorus should therefore not be regarded as necessary to the diagnosis for which the triad, tonic vomiting, great loss of weight, and visible peristalsis of the stomach, are sufficient. Special interest attaches to the case of twins, boys, one of whom developed typical pylorospasm at the age of two weeks, the other at the age of a month. The mortality, which various authors have put at 20 to 87 per cent., was in Lichtenstein's material only 4·1 per cent., and his single fatality was associated with cleft palate, which greatly interfered with the infant's feeds. His successes, achieved by dietetic and other conservative measures, are reflected in his disparaging discussion of operative treatment. He rejects the common view that pylorospasm is most frequent among breast-fed infants, and that artificial feeding is accordingly indicated. As a rule, he prefers small feeds at short intervals, i.e. 8–12 feeds of 25 to 75 grm., and he found that in some cases it was better to give human milk artificially, as sucking was apt to provoke pylorospasm. The two other principles he advocates are (1) replacement of the fluid lost in vomiting by rectal or subcutaneous injections of Ringer's solution, and (2) isolation to prevent the patient contracting influenza or any of the other intercurrent diseases responsible for many of the fatalities from pylorospasm.

**Cancer of the stomach.** R. Strauss gives the following statistics of 190 cases of undoubted gastric cancer from the Medical and Surgical University Clinic at Rostock. The paper, as Curschmann remarks in a footnote, though not containing anything really new, is of value, owing to its being based on a large number of cases. 67·6 per cent. of the cases occurred in men and 32·4 per cent. in women. No case was met with below the age of 30. 37·7 per cent. occurred between 50 and 60, and 89 per cent. between 40 and 70. According to the histories considerably more than half the cases were in persons who had previously always had healthy stomachs, their first symptoms dating back to six months at most and usually only a few weeks. About one-fifth of the cases had formerly suffered from gastric disturbance or had had their first symptoms two years previously. Examination of the acid values in 160 cases gave the following results: free hydrochloric acid was present in about 19 per cent. and absent in 81 per cent. 78·6 per cent. showed hypoacidity, 13·8 per cent. normal acidity, and 7·6 per cent. hyperacidity, 40–70 being reckoned as normal acidity, below 40 as hypoacidity, and above 70 as hyperacidity. 9 per cent. showed complete achlorhydria. 8 per cent. of the cases had developed on an old ulcer, as was shown by clinical and anatomical examination. As regards the frequency of the various symptoms, constipation was present in 60 per cent., vomiting in 60 per cent., anorexia in 71 per cent., blood in the gastric contents or faeces, including occult haemorrhage, in 64·7 per cent. In 91 per cent. of the cases which came to operation there was more or less marked emaciation. A distinctly circumscribed palpable tumour was found in 60 per cent., and a more or less definite resistance in another 21 per cent., so that only 19 per cent. of the definite cases of carcinoma showed no evidence of a tumour on palpation before operation.

Turretini and Gerber record a case of gastric cancer in a woman aged 30 which was remarkable for the fact that it never caused the slightest pain or vomiting except during a period of jaundice, when vomiting took place. The only clinical symptoms of the tumour were thrombosis of the right innominate and internal jugular veins which gave rise to considerable oedema of the face and arm, and progressive dyspnoea without any definite signs in the lungs, which suddenly developed a few days before death. The autopsy showed carcinoma of the stomach, generalized carcinoma of the pulmonary lymphatics and lungs, and thrombosis of the superior vena cava, innominate and internal jugular veins.

A case of cancer of the stomach complicated by chylous ascites is reported by Hendricks in a man aged 72 who presented enlarged glands on the left side of the neck a few weeks before death. The necropsy revealed milky fluid in the abdominal cavity, cancer of the stomach, and metastases in the liver, lungs, mediastinal glands, and the glands in the left side of the neck. The thoracic duct was dilated. Hendricks has found that at least 10 per cent. of the recorded cases of chylous fluid in the thorax or abdominal cavity or both have been due to malignant disease.

According to Vaurs, who has collected nine cases, including one of his own, perforation of the stomach is a rare complication of gastric cancer. It cannot be attributed to a special pathological form of the tumour, but it appears to be mainly due to the state of nutrition of the neoplastic tissue. Necrosis of the newly formed elements infiltrating the stomach wall takes place and a slough is formed which separates and so permits of communication with the peritoneum, into which the septic contents of the stomach are discharged. The consequences of the perforation depend upon (*a*) the point of the stomach wall where sloughing has occurred, (*b*) the rapidity with which the slough forms, and (*c*) the more or less marked reaction of the serous coat. According to the relative importance of the last two factors there occurs either a localized or a generalized peritonitis, the latter having all the appearances of an acute septic peritonitis. Massive infection of the peritoneum results, so that there is little chance of an operation being successful even if the condition is recognized at once.

From a study of the blood-sugar tolerance test in health as well as in various affections of the gastro-intestinal tract, Friedenwald and Grove have found that in gastro-intestinal carcinoma there is a rather characteristic curve of sugar tolerance which differs somewhat from that observed in carcinoma of other regions. The curve of this affection usually presents a high sugar content, even in the fasting state, followed by an initial rise up to 0·24 per cent. or higher within 45 minutes after the ingestion of the dextrose, remaining at this level for at least 120 minutes and at no time during this period falling below 0·20 per cent. The writers consider that the sugar tolerance test may render valuable assistance in a large proportion of cases, as a means of differential diagnosis between carcinoma and other diseases of the gastro-intestinal tract.

**Primary sarcoma of the stomach** forms the subject of three important papers by Koettlitz, Basch, and Haggard respectively. Although Koettlitz regards the condition as comparatively rare, only 171 cases having been collected by Gosset in 1912, Basch maintains that it is of more frequent occurrence than individual experience would lead one to infer. 244 authentic cases have been collected by Haggard, including one of his own and 13 unpublished cases from the Mayo Clinic. The condition may occur at any age, the youngest being in a boy aged 3½ years (Finlayson), and the oldest in a man of 85 (Gosset), but it is most frequent after 40. Of 66 cases in which the age is stated, 33 were in males and 33 in females.

According to Koettlitz the diagnosis has never been made until operation or autopsy, except in Westphalen's case, in which microscopical examination showed the sarcomatous nature of a portion of the vomit. In the majority of cases the diagnosis has been carcinoma. Gastric sarcoma has also been mistaken for many other intragastric and extragastric conditions, such as tumours of the spleen, tuberculous abdominal glands, abscess of the liver, suppurative peritonitis, pancreatic growth, and benign peptic ulcer with secondary infiltrating tumour. The symptoms may be so indefinite that the condition may be attributed to simple dyspepsia, and sometimes there are no gastric symptoms whatever. This is due, as Basch points out, to the fact that the mucous membrane is not involved and that usually there are no obstructive changes. As a rule there are anorexia and gastric pain, and there is always more or less considerable loss of flesh. Vomiting occurs in 20 per cent. Haematemesis and melaena are frequent, especially in the round cell variety, though less so than in carcinoma. Reports as to the gastric chemistry differ. Whereas Gosset found a complete absence of hydrochloric acid, Monti states that hydrochloric acid does not disappear till late. The only definite symptom is a tumour which was present in 66 out of 72 cases (Ziesché and Davidson). Haggard regards rapid development of anaemia and debility with loss of weight and cachexia, early rather severe and more or less persistent pain in the epigastrium, and the absence of any long-standing history of dyspepsia and pyloric obstruction, as suggestive of sarcoma. Gastric sarcoma is generally less malignant than carcinoma. According to Basch, the average duration of round cell sarcoma, which is the most malignant type, is about 15 months, that of the spindle cell type 24–32 months, and that of myxosarcoma 3½ years (see also *Medical Science*, 1920, **1**, 585–6).

According to Du Bray, of the University of California, confirmed cases of **gastric polyposis** are comparatively unusual, though he suggests that some of the vague and obscure conditions of the stomach which have been diagnosed as chronic gastritis or gastric neurosis might on further examination prove to be examples of benign tumours of the gastric wall. The term gastric polyposis includes adenomas, fibromas, lipomas, myomas, and papillomas, which may all form polypoid tumours, in some of which the connective tissue predominates and in others the glandular elements. Polyadenoma and papilloma are the most important primary benign tumours of the stomach, the others being extremely rare. Gastric polyposis is frequently associated with other morbid conditions such as gastritis, hypertensive cardiac disease, and syphilis. It is commonest in men past middle age. There are no pathognomonic symptoms, although there is sometimes suggestive evidence of the disease. Clinical manifestations depend principally on the size, position, and nature of the growth, and especially its relation to the pyloric end of the stomach. Non-pedunculated masses on the greater curvature may remain latent or more commonly produce vague epigastric symptoms followed by a desire to belch and eventually to vomit. The symptoms do not appear to have any relation to meals. The vomit contains an excessive amount of mucus, in which sometimes a polyp may be found, and enable a diagnosis to be made before operation. There is usually achylia gastrica or hypoacidity. Pedunculated growths, of which Novak reports an example, and, less frequently, non-pedunculated growths near the pylorus may prolapse and give rise to partial or complete pyloric obstruction. Haemorrhage due to the great vascularity of the growths is frequent but remains long unrecognized, occult blood being found in the fasting contents of the stomach and in the stools. The general nutrition, weight, and blood picture are less affected as a rule than in carcinoma. Long duration of the symptoms with little or no change in the general health is strong evidence against the presence of malignant disease, and should suggest the possibility of a benign tumour.

According to Neuber, three forms of **gastric myomata** may be described. The first, which is situated at the pylorus, is manifested by symptoms of pyloric obstruction which may simulate gastric ulcer or carcinoma. The second form is a subserous myoma which grows outwards into the abdominal cavity and may be mistaken for an intestinal or omental tumour on the one hand or for a tumour of the pancreas or retroperitoneal glands on the other. The third form, of which Neuber reports an example, is a pedunculated tumour which projects into the cavity of the stomach, where it gives rise to attacks of cramp and vomiting and is apt to be mistaken for gastric ulcer or cancer. Clinical examination shows occult haemorrhage and occasionally a palpable tumour.

Lemon reports a case of **angioma of the stomach** of which he has found only five other cases on record. The patient was a medical man aged 67, in whom the clinical and X-ray diagnosis was carcinoma of the stomach. In spite of a systolic blood-pressure of 220–240 and an aneurysmal dilatation of the aorta, an operation was performed and a freely movable tumour, which proved to be an angioma, was found in the fundus of the stomach. Six months after removal of the tumour the patient was in good health and engaged in his medical practice.

**Gas cysts of the abdomen.** Numerous articles have recently been published, especially by French writers such as Tuffier and Letulle, De Géry, Lenormant, Stoyanovitch, Cristol and Porte, and Weil, on the condition known as gas cysts of the abdomen, intestinal pneumatosis or cystic pneumatosis of the intestine. In this country Nitch and Shattock have described two cases under the name of diffuse emphysema of the intestinal wall. The condition is a rare one, only 70 cases having been recorded (Weil) since the first human case was reported by Bang in 1876, although a case in a healthy pig had been published by Mayer in 1825. The affection consists in the development in the abdominal cavity or peritoneum of gas-containing cysts, which are usually multiple, their size varying from microscopical dimensions to that of a hazel nut or a hen's egg. Their contents consist of a mixture of carbon dioxide, hydrogen, oxygen, and nitrogen in varying proportions. Their seat of election is the intestine, but in some instances the alimentary canal is not affected and the cysts are localized in the mesentery, omentum, or parietal peritoneum. The condition, which has been found between the ages of 13 and 67, may occur by itself, but as a rule is associated with a gastric ulcer, especially one which has reached the cicatricial or stenotic stage. Thus of 54 cases collected by Weil, in 32 there was an ulcer of the gastro-duodenal region which in 72 per cent. of the cases was stenotic. The other abdominal conditions sometimes associated with these cysts are intestinal tuberculosis, cancer of the pylorus, appendicitis, and gastro-enteritis. Owing to the variety of the symptoms, four forms of the affection have been described by Weil, viz.: (1) a pseudo-appendicular form in which the symptoms resemble appendicitis, (2) a peritoneal form simulating tuberculous peritonitis or acute perforative peritonitis, (3) a form resembling acute or chronic intestinal obstruction as in the case reported by Cristol and Porte, (4) a form simulating an abdominal tumour. Owing to the difficulties of diagnosis it is not surprising to learn that of 57 cases collected by Lenormant, 36 were not discovered till operation and 21 till autopsy. Weil, however, attaches great diagnostic value to considerable distension of the abdomen associated with a soft and easily depressible abdominal wall. Other signs which have been described as characteristic are a sensation of elastic resistance, peritoneal crepitation, abdominal transparency on X-ray examination, and the presence of gaseous ascites. Various theories, according to Stoyanovitch, have been proposed to explain the formation of the cysts. The mechanical theory that they are due to the passage of the intestinal gas into the subserous tissue is negatived by the nature of the gas, which resembles atmospheric air, and by the localization of cysts in other situations than the intestines. The theory that the cysts are tumours formed at the expense of the lymphatics fails to explain the presence of gas. The microbial theory, which appears to be the most probable, is supported by Dupraz, who isolated a liquefying coccus which on injection into a bitch reproduced the cysts in the vagina.

Singer of Vienna, describes two cases of **gastro-intestinal haemorrhage** in polycythaemia hypertonica and syphilitic aortitis respectively, and draws attention to the fact that various vascular changes associated with high blood-pressure such as arteriosclerosis and post-syphilitic vascular disease may lead to severe gastro-intestinal haemorrhage which suggests the presence of ulceration. He points out that whereas ulcers due to erosion of large blood-vessels require operation, haemorrhages due to blood and arterial diseases should be a *noli me tangere* for the surgeon, and suggests that the unexplained cases of gastro-intestinal haemorrhage described by Hale White, Reichard, and others, may be connected with disease of the blood and vascular system.

Commenting on Singer's paper, von Sohlern of Stuttgart, reports a case of intestinal haemorrhage in a woman, aged 47, in which all the ordinary causes of haemorrhage could be excluded. He emphasizes the importance in such cases of making a careful examination of the whole body, especially of the cardio-vascular system, and not only of the intestinal tract.

Fritzsche records two fatal cases of primary parenchymatous haemorrhage from the stomach in women aged 38 and 42 respectively for which no local or general cause could be found either clinically or on post-mortem examination.

Farnell and Harrington record a series of 47 cases of **acute infectious enteritis** complicated by polyneuritis, the cases being classified in three groups. In the first, which consisted of 19 cases, the gastro-intestinal symptoms were well-marked, and the polyneuritis was also prominent. In the second group, which consisted of seven cases, the gastro-intestinal symptoms were serious, and in one case fatal, but the neuritic symptoms were less severe. In the third group, which comprised 21 cases, the gastro-intestinal disturbance was the principal feature, only a few patients developing polyneuritis. Bacteriological examination showed that the condition was due to a virulent, rapidly growing staphylococcus introduced into the gastro-intestinal tract, this organism being found in the milk, throat cultures, blood, and urine. Pathologically there were acute haemorrhagic enteritis, multiple focal necroses of infectious origin in the liver, and acute haemorrhagic neuritis.

Friedman, who reports an illustrative case, classifies cases of **non-specific intestinal infection** into three groups, viz. (*a*) small intestine catarrhs, (*b*) diffuse processes involving both small and large intestine, and (*c*) colitis. The characteristics of (*a*) are meteorism, belching, and colicky pain, and, especially in involvement of the jejunum and ileum, light brown or yellowish-brown foaming acid stools with a sour odour. Continuous diarrhoea with tormina is evidence of type (*b*), and the stools become smaller and more numerous as the sigmoid and rectum become irritated. In type (*c*), while there may be alternating constipation and diarrhoea, in the more frequent irritable form there is a stubborn diarrhoea similar to dysentery, with blood in the stools and often accompanied by fever.

Antoine devotes his Paris thesis to a description of severe forms of inflammation of the rectum and colon which resemble dysentery in their symptoms and anatomical lesions but differ from it in their aetiology, which often remains undetermined. In addition to recto-colitis of syphilitic, tuberculous, uraemic, or toxic nature, there are cases in which examination of the stools shows various parasites such as lamblia, spirilla, trichomonas, *Balantidium coli*, paratyphoid and paradysentery bacilli, and salmonellae. Clinically the cases may be grouped into haemorrhagic, purulent, and mixed forms. The gravity of the attack does not appear to be due to the causal agent or to the anatomical lesions, but to the clinical course of the disease, which is characterized by repeated and profuse haemorrhage or suppuration, a protracted course and an absence of any tendency to respond to the usual treatment. The condition may last for several years with subacute intercurrent exacerbations, and does not fail to give rise to marked loss of flesh, intense anaemia, and general enfeeblement. The most frequent complication is a hypertrophic reaction of the intestinal wall giving rise to extensive stenosis of the large intestine. Complications of an infective nature are less frequent, such as perforation and peritonitis, high fever, suprarenal incompetence, joint lesions, or venous thrombosis.

The first section of Bloch's work is an attempt to clear the ground with regard to the aetiology of **infantile diarrhoea**. In his discussion of Czerny's and Finkelstein's theories, which place bacteriological activity more or less in the background, and which trace all the symptoms of infantile diarrhoea to the chemical action of the food and its decomposition products, Bloch remarks that these theories have involved their sponsors in a tangle of contraditions from which many authorities are straying back to the simpler theory of infection. Bloch qualifies his adherence to this teaching with the reservation that no irrefutable evidence has yet been produced, proving that infantile diarrhoea is due to infection.

On the assumption that this diarrhoea is due to infection, Bloch raises the further question : Is it possible clinically to distinguish between various cases of infantile diarrhoea according to their bacteriological aetiology in the same way that the diarrhoea of typhoid, paratyphoid, dysentery and paradysentery can be clinically distinguished? Bloch's material includes all the cases of acute gastro-intestinal disease in infancy observed at the Rigshospital in the period 1911–18 inclusive. The classification adopted was clinical. (1) Acute dyspepsia, with 85 cases and no deaths. (2) Acute gastro-enteritis, 310 cases with a mortality of 24 per cent. (3) Acute gastro-enteritis, complicated by chronic dyspepsia or infantile atrophy, 77 cases, with a mortality of 30 per cent. (4) Symptomatic diarrhoea, i.e. cases (figures not given) in which the diarrhoea was merely an incident of a disease outside the digestive system.

In 461 of all these cases bacteriological examinations of the faeces were made. In 21 or about 10 per cent. of all the cases of acute gastro-enteritis examined bacteriologically, paradysentery bacteria were found; these cases were scattered over several years and did not represent a single epidemic. In one case typhoid bacilli, and in five cases paratyphoid bacilli were found; but these, too, were isolated cases, not the result of a single outbreak. The clinical manifestations of 21 cases of paradysentery varied greatly; some were severe and some were exceedingly mild. In 14 out of 18 cases of acute paradysenteric gastro-enteritis, blood was demonstrable in the motions, but there were many other cases of haemorrhagic motions in which paradysentery could be excluded. The clinical course of the six typhoid or paratyphoid cases was more uniform. In every case the onset of the disease was sudden, and the diarrhoea and vomiting were accompanied by slight fever. Apart from the bacteriological evidence in these cases, there was no sign of typhoid fever, such as a roseola or enlargement of the spleen. The clinical picture was that of mild, non-specific gastro-enteritis. The *B. proteus* was found in 52 out of 128 cases of acute gastro-enteritis and in 95 out of 244 cases of acute dyspepsia and symptomatic diarrhoea. Bloch concludes that the clinical picture, epidemicity, and the pathological-anatomical findings in infantile diarrhoea are the same whether pathogenic bacteria are found in the faeces or not. Acute gastro-enteritis in infancy is due to infection, but not to any specific infection. In most cases coliform bacilli, not pathogenic to adults or children over a certain age, are probably the cause of this disease. In a minority of cases the disease is due to micro-organisms pathogenic to adults.

Pseudo-ascites in children suffering from prolonged enteritis seems to have been first described by Tobler in 1914, and other reports of the syndrome have appeared since. Segagni now reports four cases in which were present (*a*) very chronic diarrhoea, (*b*) enlargement and flattening of the abdomen, (*c*) some degree of fluctuation and shifting dullness, and (*d*) very large amounts of fluid in the bowel, but no excess of peritoneal fluid. The children were all wasted and cachectic and the general appearance closely simulated tuberculous peritonitis, for which several recorded cases have been operated upon. Cure appears to be long and tedious and is not specifically dealt with by Segagni.

Bársony records two cases in which an extreme **elongation and dilatation of the colon** gave rise to difficulty in swallowing, owing to pressure on the subphrenic portion of the oesophagus. In the first case, which occurred in a man aged 54, the condition of the colon was found to be secondary to carcinoma of the rectum, which had hitherto not caused any symptoms. After colostomy in the lower part of the descending colon the dysphagia disappeared. In the second case, which occurred in a man aged 40, the dilatation of the colon was apparently due to intestinal paresis following enteritis, and was cured by a course at Carlsbad.

**Treatment.** The following modification of Sippey's method of treatment of gastric or duodenal ulcer has been adopted by Hurst: 5 oz. of milk (or preferably milk and cream in equal quantities) are given every hour from 8 a.m. to 8 p.m. inclusive. To each feed gr. x of sodium citrate dissolved in 2 drachms of emulsio magnesiae are added. Immediately before alternate feeds, beginning at 7.30 a.m., $\frac{1}{2}$ oz. of olive oil is taken. This inhibits the secretion of gastric juice and also supplies a digestible and absolutely unirritating food of very high nutritive character in a concentrated form. Immediately before the remaining feeds ɱv tinct. belladonnae, which has a similar inhibiting effect, are given, as oil before each feed sometimes gives rise to nausea. Half an hour after each feed, and at 9, 9.30, and 10 p.m., a powder containing gr. x calcium carbonate and gr. xxx bismuth carbonate is taken in a little water. At 6 a.m. $\frac{1}{2}$ oz. of bismuth carbonate, shaken up but not suspended in 5–10 oz. of water, is swallowed and the patient then lies on his right side or in such a position that the bismuth comes in contact with the ulcer. This forms a protective covering to the ulcer and at the same time neutralizes any acid present and calls forth a secretion of protective mucous. The stomach contents are thus kept neutral or alkaline from 6 a.m. to 10 p.m. At 11 p.m. the stomach is completely emptied by Senoran's evacuator; if not more than 2 oz. are present on two consecutive nights, this can be discontinued. If half a pint or more is removed at 11 p.m., the stomach should be evacuated again at 1 a.m. At 11 p.m. atropin sulphate gr. $\frac{1}{50}$ is injected subcutaneously to inhibit the further secretion of gastric juice. At the same time the alkaline powder should be repeated every two hours through the night. This treatment should be continued until for three weeks the patient has had no spontaneous pain, no trace of tenderness has been present, no occult blood has been found in the stools, not more than 2 oz. of fluid have been removed on any one evening, and the X-rays showed no evidence of active ulceration. The diet can now be rapidly increased until at the end of a week everything is taken with the exception of chemically irritating substances, such as alcohol, vinegar, mustard, pepper, pickles, &c.

Various physicians, such as Hurst in England, Albu in Germany, and Bastedo in America, deprecate surgical interference in the treatment of gastric or duodenal ulcer until a thorough medical treatment has been tried, on the grounds of the risks of the operation, the tendency to recurrences and unpleasant after-effects, such as hernia, rectus diastasis, gastro-intestinal fistula, and peritoneal adhesions. Albu remarks that the majority of patients in whom the operation has been unsuccessful do not return to the surgeon but consult a physician, especially if a long time has elapsed since the operation without improvement taking place. Bastedo maintains that a case should only be regarded as surgical when it continues to show (1) persistent recurrent haemorrhage even small in amount; (2) pain; (3)

nausea; (4) pylorospasm of such persistence as to simulate pyloric stenosis; (5) inability to ingest comfortably ordinary wholesome foods or to take enough food to maintain nutrition while leading a normally occupied life; (6) recurrence after an apparent cure. Other indications for operation mentioned by Hurst and Albu are perforation, hour-glass contraction, chronic peritoneal adhesions, and the possibility of a growth being present.

Crohn and Reiss studied the effects of restricted or so-called ulcer diets on gastric secretion and mortality, and found that only a small percentage reacted to medical treatment by showing a reduction of acid produced during digestion. Clinical improvement, however, took place independently of whether the hyperacidity was relieved or not. A similar conclusion was arrived at with regard to hypersecretion, as improvement occurred as often in cases with persistent hypersecretion as in those relieved of their excessive flow of gastric juice, and was apparently not dependent upon it. As regards the relationship between improved gastric motility and clinical relief, in 11 out of 13 cases of delayed motility treatment alleviated this symptom and reduced the emptying time to normal. All these 11 cases were also freed from subjective complaints. No explanation could be given of the relief of symptoms in cases not complicated by delayed motility in which the hyperacidity and hypersecretion were not affected by treatment.

Eight benign cases of impermeable cardiospasm, by which is meant failure of food to enter the stomach in the normal way, absence of organic stricture, and impossibility of reaching the stomach by the usual gastric tube or bougie, were treated by Einhorn (2) with retrograde stretching of the cardia soon after a previous course of duodenal alimentation. The stretching is done first by the pyloric dilator, every other day or twice a week, the dilator being introduced at bed-time supplemented by a dose of atropin and the stretching done the following morning. After a few stretchings the dilator enters the stomach in a much shorter time.

Einhorn (3), who had previously recorded a case of duodenal perforation successfully treated by duodenal (jejunal) alimentation, reports another successful case in a man aged 50. After three weeks of jejunal alimentation the tube was pulled up to some extent, so that the capsule end was situated in the duodenum proper. It was found that duodenal alimentation suited the patient much better, as he did not lose weight as he did on jejunal feeding.

According to Bensaude and Vicente, rectal injections of a solution of extract of bile causes an increase of peristalsis in the terminal portion of the large intestine, resulting in the evacuation of the contents of the rectum and sigmoid. This action is purely excitomotor and is not accompanied by any excess of intestinal secretion. The use of bile enemata is therefore indicated in temporary or habitual constipation when single enemata or laxatives are ineffective. Powdered bile in doses of 4–5 grm. in $\frac{1}{4}$ litre of water does not produce any rectal pain or irritation, even when employed for several weeks, and its habitual use does not interfere with its efficacy.

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## DIPHTHERIA

**Epidemiology.** Dubourg and Guénard give statistics showing the mortality from diphtheria at the Children's Hospital at Bordeaux during the thirty years 1888–1917. In 1888 and 1889 the cases were nursed in a general ward with an average mortality of 49 per cent. and a maximum mortality of 54 per cent. in 1888. From 1890 to 1893 the cases were admitted to a special block, and there was a decided fall in the mortality, since it was 35 per cent. during this period. In 1894, with the creation of separate cubicles for each patient, it fell to 19·4 per cent., the lowest figure reached before the introduction of antitoxin. Since 1895, when antitoxin was first employed, the average mortality has been 7·28 per cent. with a maximum of 15·5 per cent. in 1899–1900, and a minimum of 1·53 per cent. in 1907 (3 deaths among 195 cases). The number of operations for laryngeal diphtheria has also fallen considerably; in 1894 56 per cent. of the admissions required tracheotomy. After the introduction of serum and before intubation became current the annual average of tracheotomies fell to 9·87 per cent. of the admissions. After the introduction of intubation the number of operations including both intubation and tracheotomy was 15·34 per cent. of the admissions.

Huntemüller records an epidemic of diphtheria in the 19th Bavarian Infantry Regiment fighting in Lorraine, and considers the causes of the outbreak to be as follows: (1) the general diminution of resistance due to the hard work involved in building the trenches, insanitary quarters, and bad weather; (2) the local irritation of the chalk dust produced while working. After the trenches had been completed there was a steep fall in the morbidity. That this was the effect of increased resistance of the troops and not the result of a diminution of the infectivity or virulence of the diphtheria bacilli was shown by the large number of carriers who were subsequently discovered and by the occurrence of a fatal case.

**Aetiology.** In view of Savage's recent contention that there is no foundation for the popular belief that cats may suffer from diphtheria (vide *Medical Science*, 1920, **2**, 358–9), the case reported by Simmons is of considerable interest. The patient was an elderly lady who developed a fatal attack of faucial diphtheria after fondling a cat which had been ill one week before her illness began. The cat was said to have had a croupy cough, to have been unable to swallow food, and to have become very thin. Throat cultures from the cat and from the patient showed morphologically similar organisms resembling diphtheria bacilli, and their virulence for guinea-pigs was the same. The cat was killed, and a post-mortem examination revealed a small ulcer covered with a yellowish membrane on the upper surface of the left nasal fossa, cultures from which yielded diphtheria bacilli. No lesions in the internal organs were found. A second cat which had played with the first and yielded a throat culture showing morphologically typical diphtheria bacilli, died after eight days' confinement in a cage and *post mortem* showed small membranous patches on the vocal cords, from which virulent diphtheria bacilli were grown. The history of contact, dates of infection, and bacteriological findings suggested that the first cat was the source of infection of the patient as well as of the second cat, though this could not be absolutely proved. It was certain, however, that both cats were carriers of virulent diphtheria bacilli and were therefore a danger to human beings.

Cartesegna and Casassa of Turin, examined catheter specimens of the urine in 100 cases of diphtheria and found diphtheria bacilli present in 85 per cent. They are convinced that, by slight improvement of technique and frequent examination of a larger quantity of urine, positive results could be obtained in all cases. The presence of the bacilli was independent of the severity of the case. It was impossible, for obvious reasons, to continue investigations on the same individual until the examination became negative, but it was an almost invariable rule for the urine to be still positive one and a half months after the onset of the attack, when the faucial cultures were negative. The diphtheria bacillus was never found in pure culture in the urine, but always in association with other micro-organisms, such as the streptococcus, *B. coli*, pneumococcus, the Brisou coccus, and Friedländer's bacillus. The practical importance of these observations is that excretion of diphtheria bacilli in the urine should be taken into consideration in dealing with carriers.

**Symptomatology.** A case of isolated *diphtheria of the mouth* in a breast-fed infant, aged 14 days, is reported by Janssen from the Göttingen University Children's Clinique. The region affected was the alveolar margin of the upper jaw on either side of the mid-line. Diphtheria bacilli were found in cultures of the lesions, whereas nasal and faucial cultures were negative. 2,000 units of antitoxin were injected and the condition rapidly cleared up. Though secondary diphtheria of the mouth, which usually appears in the form of ulcers, is well known, Janssen has been unable to find any record of a case of primary diphtheria of the mouth.

According to Lambert, primary *diphtheria of the middle ear* is observed in both sexes, and in adult life as well as in childhood, though like all forms of diphtheria it is commonest in early life. Infection takes place from the pharynx or nasal fossae by the Eustachian tube. The condition is characterized by the association of the following three symptoms: intense and persistent pain, pronounced bulging of the tympanic membrane, and a sero-haemorrhagic discharge, sometimes containing whitish-grey pieces of membrane. If recognized in time and treated by antitoxin the condition rapidly clears up, especially if it is not complicated by a secondary infection, but if it is not recognized or treated until late, it tends to become chronic and to be complicated by mastoiditis or facial paralysis, which may even occur during the first few days, so that primary diphtheria of the ear cannot be regarded as a mild form of ear disease.

Although *diphtheria of the vulva* is relatively frequent in small children, usually secondary to faucial diphtheria, this localization is extremely rare in adults. Kromayer of Berlin, reports a case in a woman aged 22, who, in May 1919, had contracted syphilis, for which she was treated with salvarsan and mercury. When she was seen in the following August she presented a profuse yellow vulvar discharge and several ulcers round the clitoris and urethral orifice which were regarded as soft chancres. The ordinary treatment for this condition had no effect, and the ulceration became more extensive. When the patient was seen by Kromayer, on November 5, the floor of the ulcer was covered by a thick white adherent membrane, smears from which showed diphtheria bacilli. 3,000 units of antitoxin were given, and within three weeks the ulceration had completely healed. There does not appear to be any similar case on record of vulvar diphtheria simulating soft chancre.

Leendertz of the Königsberg University Medical Clinique, records a case of primary *diphtheria of the vagina and skin* of the intergluteal folds in a child aged 5½ years, in whom nasal and faucial diphtheria were absent. A brother and sister of the patient had recently suffered from diphtheria. The truth of Trousseau's doctrine that diphtheritic paralysis begins in the region first attacked by diphtheria was exemplified in this case. The first paralysis occurred in the bladder, as was shown by incontinence of urine, on the ninth day after disappearance of the membrane, and was followed by paralysis of the rectum (incontinence of faeces) eighteen days later, or on the forty-eighth day of disease. On the forty-ninth day paralysis of the palate, third and sixth cranial nerves, and ataxia of the legs were observed. All the palsies gradually disappeared. The origin of the bladder palsy in this case can be explained as in the case of palatal palsy after faucial diphtheria by a direct ascent of the toxins. The subsequent palsies are regarded by Leendertz as the result of toxins circulating in the blood, when, according to recent investigations, they may persist for a long time, especially in the lungs.

Peiper, alluding to the frequency of vulvar and cutaneous diphtheria during the war, attributes this occurrence to defective cleanliness of the skin, which was chiefly due to the absence of soap.

After noting that *diphtheria of the umbilicus* was first described in 1860 by a Norwegian, Möller, whose patient, a new-born child, died after an illness of 12 days, Schönfelder gives an account of an important epidemic observed in Christiania in 1919. The first case was that of an infant, born on April 13 at a maternity hospital, and admitted to Ullevaal Fever Hospital on May 10. The diphtheritic nature of the umbilical inflammation was not recognized till after death, on May 28, when diphtheria bacilli were found. The necropsy showed no sign of peritonitis apart from a limited patch of redness and hyperaemia on a part of the large intestine situated immediately beneath the umbilicus. Between May 19 and November 15, 130 patients were admitted from the maternity hospital to the fever hospital, of whom 33 were infants with umbilical diphtheria. These cases were grouped in four classes according to the severity of the disease, 10 being in the first class, 19 in the second, and 2 in each of the last two classes. In the first class the condition of the umbilicus, from the clinical standpoint, was practically normal. The diagnosis depended on the routine bacteriological examinations of the umbilicus which, during the epidemic, were undertaken at the maternity hospital. These cases may, therefore, be regarded as 'carriers'; as they were at once treated with antitoxin, it is impossible to say whether they would subsequently have developed into clinically demonstrable diphtheria or not. In the second class, indolent ulcers, up to the size of a small coin, were coated with a greenish-yellow discharge, but not with a typical pseudo-membrane. In the remaining two classes there was extensive infiltration and an erysipelas-like redness about the umbilicus which formed an ulcerating prominence as large as a Spanish nut. The depth of the ulceration in one of the cases in the fourth class was so great that the patient's escape from peritonitis was remarkable.

Discussing the frequency of umbilical diphtheria, Schönfelder points out that, as the disease is seldom clinically distinguishable from non-specific infections, it must often be overlooked. Every infection of the umbilicus, especially during an epidemic of diphtheria, should, therefore, be suspect, particularly if the infant snuffles. It is curious that while severe diphtheria of the throat often kills the patient in a few days or a week, diphtheria of the umbilicus lasts several weeks, and for a considerable time does not disturb the general health. Even in the one case which terminated fatally the duration of the disease was 30 days. The disease is seldom febrile, and only in 3 out of the 33 cases was the temperature raised. The absence of fever was particularly remarkable in the worst cases, and this point is of value in the differential diagnosis, for in non-diphtheritic infections the height of the temperature is directly proportional to the severity of the local reaction. In 2 cases diphtheria bacilli were also found in the nose, and in 3 in both nose and throat.

Reviewing his own experience and others, Schönfelder concludes that, in severe cases, the prognosis is bad without antitoxin. He gave 4,000 units and, in the worst cases, 6,000 units. Remarking on the fact that no case of umbilical diphtheria has been reported in Norway between 1861 and 1919, Schönfelder finds it strange that in this year many cases should have occurred both in Bergen and Christiania. He correlates these outbreaks with a sudden rise in the frequency of diphtheria of the skin in 1919. Thus, in 1916, among 912 notifications of diphtheria, there was only 1 of skin infection. In 1917 there were 5 such cases among 926 notifications, and in 1919 there were 32 among about 1,700 notifications. It is also instructive that in 1860 the occurrence of umbilical diphtheria coincided with many cases of wound diphtheria. As to the source of infection at the maternity hospital, no 'carriers' could be found on its permanent staff, but some of the mothers were found to be infected on admission.

Looft, who records two cases of diphtheria in the new-born, in one of which the umbilicus was affected, maintains that diphtheria is not, as commonly supposed, rare in the new-born. It should always be suspected in the presence of snuffling, otitis, lesions of the skin, and, not least, inflammatory conditions of the umbilicus. In his first case, a new-born infant was infected by another child in the same family, suffering from nasal diphtheria. The infant's snuffling was regarded by the parents as a simple cold, and, as it seemed well in other respects, medical aid was not sought. After about three weeks numerous paralyses developed in rapid succession; the muscles of the neck and those supplied by the lower branches of the facial nerve were involved, as well as all four limbs. There was absence of tendon reflexes with anaesthesia and, in two places, hyperaesthesia. This polyneuritis might well have led to the diagnosis of Heine-Medin's disease, had not diphtheria bacilli been found in the nose. No antitoxin was given, and only palliative measures were adopted. Death occurred after eight days' illness, when the child was about five weeks old. The chief interest attaching to the second case, one of umbilical infection, was the promptness with which the patient recovered after the injection of 650 units of antitoxin supplemented by compresses of Burow's solution. It transpired that the mother had recently suffered from 'a cold', and diphtheria bacilli were found in her throat. They were still there a month later.

After referring to five cases of umbilical diphtheria observed by Axel Looft in 1919 at a maternity hospital in Bergen, C. Looft discusses the clinical picture and remarks that its uniformity, as taken for granted by the follow-my-leader writers of text-books, is purely hypothetical. Umbilical diphtheria is in reality extraordinarily polymorphous, and apart from bacteriological findings, there is nothing constant. The same applies to wound diphtheria, which shows every degree and kind of inflammation from phlegmon and gangrene to a reaction which is so slight that only the bacteriological examination clinches the diagnosis.

Göppert states that the great majority of cases of diphtheritic infection of the umbilicus occur at the end of the first week of life or in the course of the second week. The disease may, however, develop much later. In such cases the child may be suffering from nasal diphtheria or be a diphtheria carrier, so that the infection may have arisen in a lying-in hospital. A larger proportion of the cases, according to Göppert, show hardly any symptoms. A slight dampness of the umbilicus may prompt an examination which shows a thin deposit in the folds of the umbilicus or on the granulating umbilical wound. In other cases, especially those in which the infection occurs in the first few days of life, the disease runs a much more malignant course even from the first. Ulceration, with infiltration of the surrounding areas, occurs, and even gangrene of the navel may develop. Most cases of diphtheria of the umbilicus, like diphtheria of the new-born, generally originate in lying-in hospitals, though the infection may sometimes occur in a private house.

Henkel, who records four illustrative cases, agrees with von Reuss, who, in his text-book on diseases of the new-born, states that diphtheria of the umbilicus does not present a characteristic or specific appearance, and that the diagnosis must be made by bacteriological examination, which should be carried out as soon as possible. Diphtheria of the umbilicus may be associated with diphtheritic processes elsewhere, e. g. in the nose, conjunctiva, skin, &c., but this is not necessary, and it is usually the only localization of diphtheria, as in the cases reported by Henkel. The general condition is not affected at first, and it is only when the disease has made considerable progress that constitutional disturbance takes place. As a general rule, in Henkel's experience, diphtheria of the umbilicus is not a severe infection, provided it is recognized early before a mixed infection occurs.

Prausnitz records five cases of diphtheria of the umbilicus, four of which occurred in new-born children and three of which were fatal. In the first case death was due to generalized paralysis, in the second to staphylococcal peritonitis, secondary to the umbilical infection, and in the third to debility resulting from concurrent nasal and umbilical diphtheria.

Snell reports eight cases of diphtheria of the umbilicus from the Göttingen University Children's Clinique. Three of these had severe, two moderate, and three mild attacks. Death, which was sudden, occurred in three cases, being due in one case to erysipelas, and in the other two to broncho-pneumonia. Paralysis of any kind was not observed. Concurrent nasal diphtheria was present in five cases. In two cases pyogenic organisms were found, in one in the blood, and in the other in a section of the umbilicus. In three cases the disease occurred in the first few days of life, and in the others in the second week or as late as the fourth week.

At the Greifswald Medical Society on June 20, 1917, Peiper showed a case of diphtheria of the penis and umbilicus in a new-born infant. Diphtheria bacilli were also found in the nose and throat, without, however, any clinical evidence of disease in these regions. The source of infection was the mother, who was suffering from intertrigo in the secretion from which diphtheria bacilli were present. Peiper also alluded to the frequency of diphtheria carriers among the new-born, no less than 36 per cent. of the children admitted to an infant's home being found to be carriers.

Wieting maintains that *wound diphtheria*, on which so much has recently been written (vide *Medical Science,* 1919–20, **1**, 151–4 ; 404–9), is simply the old hospital gangrene which was by no means uncommon in the military hospitals in the campaign of 1870–1, but under the influence of the aseptic and antiseptic methods of peace time had become practically unknown.

A case of diphtheria, with multiple and subintrant *relapses,* is reported by Boidin. The patient was a soldier who had an attack of diphtheria which was treated in the ordinary way. After the acute symptoms had subsided he remained well for six weeks and then developed a condition of chronic sore throat with periods of transient improvement. It was not until five months had elapsed that the sore throat, which had been regarded as herpetic angina, was recognized as diphtheria and treated as such. After remaining well again for six weeks the patient had another relapse, eleven months after the initial attack, and infected other soldiers.

E. Aaser has attempted to calculate the incidence of *heart failure* in diphtheria by comparing the deaths with the actual number of cases treated at Ullevaal Fever Hospital at various periods. He classifies his cases in four groups, according to the severity of the disease, and he excludes from his analyses cases complicated by other diseases, as well as 'carriers'. In the pre-serum period, 1890–4, there were 858 cases in the first group with only 8 deaths. In the second group there were 245 cases with 48 deaths. In the third group there were 89 cases with 55 deaths. In the fourth group there were 30 cases with 27 deaths. Thus the mortality percentages for the four groups were 1, 20, 70, and 90 respectively. Comparing these figures with those for 1915–18, he shows that in the first two groups there were no deaths, in the third group the mortality was only 1 per cent., and in the fourth group only 19 per cent. The total number of cases in this 4-year period was 1,856. Thus, the mortality among the fourth group cases treated with serum was practically the same as that for the second group cases treated without serum. But though serum treatment has thus greatly reduced the mortality, it has, in Aaser's opinion, done little or nothing to reduce the incidence of cardiac complications late in the disease. He even thinks that these may be promoted by the serum on account of its high carbolic acid content (0·5 per cent.). He gives no figures indicating the frequency of non-fatal cardiac complications, but he suggests that if physicians dared undertake functional heart tests on their patients on the day of discharge a very large proportion would react with signs of cardiac insufficiency. The treatment he recommends is absolute rest, with morphia to combat restlessness and insomnia in children as well as adults. An ice-bag over the heart, laxatives, and flushing the system with fluids are also recommended.

Marriott reports a case of post-diphtheritic *paralysis* of the respiratory muscles in a girl aged 10 years, whose life was saved by prolonged artificial respiration. An apparatus designed by Gesell and Erlanger for administering artificial respiration to animals was used and was employed at intervals for five days, at the end of which time the respiratory muscles had so far regained their function that artificial respiration was necessary only at relatively infrequent intervals. Complete recovery took place.

From a study of the literature and observation of six cases of diphtheritic paralysis, in which examination of the cerebrospinal fluid was made, De Lavergne comes to the following conclusions : (1) Diphtheritic paralysis, whether confined to the soft palate or generalized, is accompanied, as a rule, by a meningeal reaction. (2) This reaction consists in an excess of glucose and albumin in the cerebrospinal fluid with a normal lymphocytosis. (3) This reaction is probably present a little before the appearance of the paralysis. The excess of glucose in the cerebrospinal fluid is the first sign, and persists until clinical recovery.

Diphtheritic paralysis of central origin, of which Riemschneider reports a case, is very uncommon. In 1913 Rolleston (1) collected 80 cases of *diphtheritic hemiplegia*, including six of his own, in patients aged from 1½ to 17 years. Right hemiplegia occurred in 48—in 21 of whom aphasia was noted—left in 27, and in 5 no details were given. The occurrence of the hemiplegia took place at the following dates : in the first week 1 case ; in the second week 14 ; in the third 27 ; and in the fourth to the seventh 12. In 14 cases in which no exact date is given it is said to have developed in convalescence ; in 12 no date whatever is given. Recovery took place in 52, death in 24, and in 4 no details were given. Necropsies were held in 18 cases. Embolism was found in 13, thrombosis in 3, haemorrhage in 1, and sclerotic atrophy in 1. In all the cases where details are given the initial attack was severe. Albuminuria and ordinary diphtheritic paralysis developed in a large number. The prognosis in diphtheritic hemiplegia, as in hemiplegia generally following acute infections, is unfavourable as regards complete recovery. In the great majority of cases contractures and atrophy have supervened in the paralysed limbs. Rolleston (2), however, has recently reported two cases of diphtheria in which the hemiplegia, though complete and accompanied by aphasia and characteristic changes in the reflexes, disappeared within 24 hours. Though one case recovered and an autopsy could not be obtained in the other, which proved fatal, it is probable that uraemia was the cause of the paralysis in one case and minute emboli in the other.

**Diagnosis.** Hesse of the Halle University Medical Clinique, describes an auscultatory sign for diagnosing laryngeal diphtheria which, in the absence of concomitant faucial involvement, can only be recognized by laryngoscopy or the presence of diphtheria bacilli in the sputum. Hesse's sign consists in the normal bronchial breathing being replaced by extraordinarily rough and sharpened breath sounds. The phenomenon, which is present not only in laryngeal diphtheria accompanied by stridor or recession, but also in the non-stenotic form of the disease, is best heard over the lateral aspect of the thyroid cartilage or over the cricoid or upper rings of the trachea.

**Prophylaxis.** The determination of susceptibility to diphtheria by the Schick test, and the immunization of those found to be susceptible by toxin-antitoxin, have formed the subject of numerous recent papers. Bauer, who is in charge of Schick testing and active immunization for the Philadelphia Department of Health, has made observations on 3,000 children with the following results: up to six months infants enjoyed immunity, from six months to three years 72·5 per cent. were positive, from three to five years 46 per cent., from five to ten years 32·4 per cent., from ten to twenty years 28·2 per cent., and over twenty years 13·2 per cent. 1,100 persons who were found to be susceptible to diphtheria by the Schick reaction were given toxin-antitoxin. 200 of these were retested at the end of five months, and all gave a negative test. A reaction due to the protein contained in the mixture occurred in a few individuals and consisted in malaise, headache, fever up to 101–3°, joint pains, and leucocytosis. The reaction usually occurred after the first injection, and was milder after the second or third dose, if it occurred at all.

Blau studied the Schick test and active immunization against diphtheria with toxin-antitoxin at the Stuyvesant Clinic of the Department of Health, and found that more than a third of the children under 14 were susceptible to diphtheria, i. e. had no natural immunity against the disease. The greatest susceptibility was between 1 and 6 years. After the age of 6 years the degree of susceptibility gradually diminished, as shown by the negative Schick tests. Of a total of 227 negative Schick tests 136 were between 6 and 14 years. Blau considers that the immunity produced by three injections of toxin-antitoxin is probably permanent. The development of an active immunity is determined by the Schick test at the end of three months. If the test is negative, the person is immune. By re-injecting those who give a positive test an immunity can be developed in all susceptible persons. Blau, however, points out that, as the immunity afforded by toxin-antitoxin does not develop until the lapse of from two to twelve weeks, active immunization with toxin-antitoxin cannot be utilized to protect persons within that period.

Owing to an outbreak of diphtheria in a state industrial school, Lilly performed the Schick test on 257 persons aged from 15–21, and obtained positive results in 148 and negative in 109. The susceptible ones were then given three doses each of 1 c.c. toxin-antitoxin at intervals of seven days. In only 33 per cent. was there any general reaction, and in a much smaller number a slight local reaction. The general disturbance was much less after the second dose, and almost nil after the final injection. Two months later all the boys who had had the toxin-antitoxin were given a second Schick test, and out of 98 only 18 showed a slight reaction after 72 hours, and 13 showed a very slight pigmentation at the end of a week. A third test was performed three months after the immunization, when only six showed a slight reaction. Two boys contracted diphtheria after two injections of toxin-antitoxin, and one on the day following the last injection. These cases were treated with ordinary antitoxin and recovered promptly. Lilly concludes (1) that toxin-antitoxin gives absolute immunity to diphtheria when more than one month has elapsed after its administration; (2) that it does not cause such troublesome and alarming reactions as ordinary antitoxin often does; (3) that the immunity persists indefinitely. He points out, however, that toxin-antitoxin has no curative properties and does not immediately protect against diphtheria, and that the Schick test is not rapid enough to be of immediate use in cases exposed to clinical diphtheria, and should be employed only to separate immunes from non-immunes.

Armand-Delille and Marie investigated Schick's test in more than 200 children belonging to several orphanages and obtained positive results in 75 cases, or 37·5 per cent. They found that in children of the same family the reaction was almost always the same, and that it was negative in healthy carriers.

Renault, while emphasizing the importance of Schick's reaction in the epidemiology and prophylaxis of diphtheria, points out that it does not render unnecessary the investigation and isolation of carriers, as these are to be found both among those who are susceptible and those who are refractory to infection by diphtheria.

Leete examined the Schick test in 500 cases of scarlet fever and found positive results in 57·2 per cent. Positive reactions diminished with increasing age, but were more frequent among scarlet fever patients than normal adults of the same age. In a series of normal adults only 17, or 28 per cent., were positive as compared with 37·5 per cent. in a corresponding group of scarlet fever patients. Of 32 diphtheria cases Leete found that 18 were negative and 14 positive to the Schick test, this fact showing that immunity may depend on other factors than the presence of antitoxin.

From a study of Schick's test in cases of diphtheria, non-diphtheritic angina, and diphtheria carriers among soldiers, Rieux and Zoller recommend that the test should be performed on every new recruit and the result noted in the soldier's book, only those with a positive reaction requiring immunization.

De Lavergne and Zoeller report four cases of diphtheritic paralysis with a negative Schick's reaction. This shows that even in a state of active immunity gradually conferred by an attack of diphtheria the antitoxin, which is in a sort of nascent condition, does not succeed in neutralizing the toxin fixed in the nerves.

Park states that in 95 per cent. of the cases injected toxin-antitoxin gives an immunity, which develops between the fourth and twelfth week and persists for at least three and a quarter years. He mentions that the injections are absolutely harmless, 1,950 babies from three to five days old having been injected without any ill effects. The older the patient the more severe the reaction, this being due to the presence of peptones and other foreign products in the broth and not to the toxin-antitoxin itself. The method of administering the toxin-antitoxin recommended by Park is injection of 1 c.c. subcutaneously or intramuscularly with the finest needle.

As the result of a recent inquiry Bieber has found that inoculation with toxin-antitoxin in the Magdeburg district in 1913 conferred a definite if not absolute immunity against diphtheria, the results being sufficiently encouraging to make a more extensive use of the method in districts exposed to diphtheria advisable.

The gist of A. H. Meyer's paper is in the question: Does diphtheria break out so frequently in children's wards as to warrant special prophylactic measures? Since the writer's clinic was started, in July 1905, about 2,400 patients have been treated, the average number of occupied beds out of 24 being 20. During the following 14 years, 28 cases of diphtheria developed in the hospital. In the first 10¾ years there were only 7 cases among 1,700 patients, whereas in the last 3 years there were 21 cases among only 700 patients. Since March 1910 every patient was examined on admission for diphtheria bacilli, and in this way 21 'carriers' were detected and prevented from spreading infection. Up till March 1916 the writer flattered himself that his comparative immunity from outbreaks of diphtheria was due to these precautions. His more recent experience convinced him that even when the nose as well as the throat is examined for diphtheria bacilli, and the examination is repeated a week later, 'carriers' are still able to elude detection in a certain proportion of cases. But though his measures proved imperfect, the fact that he did intercept 21 'carriers' has convinced him that this system of examining all admissions for 'carriers' is useful. As for the procedure to adopt when diphtheria has already broken out, he used to give prophylactic injections of serum till nine years ago when, for fear of anaphylactic shock, he abandoned this treatment. Of the wisdom of this course he is still in doubt.

**Treatment.** In a review of 25 years' antitoxin treatment Martin states that in the pre-antitoxin era the highest mortality from diphtheria per 100,000 inhabitants was 200 deaths (Berlin 1883) and 100 (Paris 1882): since the introduction of antitoxin the highest mortality for Paris was 27·7 deaths per 100,000 during the epidemic of 1901–2. The minimum figures were 6·4 per 100,000 for Paris in 1906, 3 per 100,000 for Havre in 1908, and 2·6 per 100,000 for Utrecht in 1908. As a general rule, before serum therapy, the average mortality per 100,000 below 100 was above 50. Since serum therapy had been introduced the average number of deaths had been almost always less than 20, and often less than 10 per 100,000 inhabitants.

*Hospital statistics.* During the years 1890–93 inclusive, of 3,971 cases admitted to the diphtheria block of the Hôpital des Enfants Malades, 2,029 died—a mortality of 51·75 per cent. In cases treated by serum from February to July 1894 the mortality was 24·5 per cent. The lowest death-rate in this hospital was reached in 1904, when Marfan and Le Play reported a mortality of 7·4 per cent. Before serum treatment the average mortality of faucial diphtheria was 34 per cent,; since the introduction of serum it has been about 10 per cent. The mortality from operations for laryngeal diphtheria, which was previously 73 per cent., is now about 20 per cent., and the number of operations required has considerably diminished. In the years 1887–94, 36 per cent. of the admissions required operation; since then the number of operations has fallen to less than 15 per cent.

At the Pasteur Hospital, 1,624 cases have been admitted from 1900–19, with 133 deaths, or a mortality of 8·18 per cent. As a general rule the mortality at this hospital has ranged between 10 and 15 per cent., or more than two-thirds less than in the pre-antitoxin era.

*Diphtheria in the army.* Before serum treatment diphtheria was rare in the French army. According to Bayeux, from 1888–94 there were 3,551 patients and 393 deaths, or an average mortality of 11·07 per cent. In 1895 and 1896 the mortality fell to 5·65 per cent., and in 1897–1914 was only 3·3 per cent. During the five years of the war, in the Army of the Interior, i. e. in the hospitals situated outside the zone of the armies, there were 15,271 patients and 378 deaths, or a mortality of 2·4 per cent. In the zone of the armies there were 11,433 cases and 229 deaths, or a mortality of 2 per cent.

*Diphtheria mortality in Paris.* Before the introduction of serum 1,432 persons died annually in Paris from diphtheria, whereas during the last few years this figure has dropped to 130. Before serum treatment the maximum number of deaths a week was 45 and the minimum 14; since 1898 the maximum number of deaths was 20 in 1898, and the minimum 1 in 1918.

The intramuscular route for injection of antitoxin, widely employed in Germany and the United States and recommended in this country by Ker and Rolleston and Macleod, has recently been adopted by French physicians such as Netter, Weill-Hallé, and Armand-Delille. Weill-Hallé agrees with Rolleston and Macleod, who had claimed the following advantages for the intramuscular method: (1) It is quite as simple as the subcutaneous method, ensures more rapid absorption, and is less liable to give rise to abscesses at the injection site. (2) It is superior to the intravenous method not only in the greater simplicity of its technique, but also in the less rapid excretion of antitoxin after injection. (3) The more rapid absorption of antitoxin by the intramuscular route is shown by lesser incidence of paralysis, especially of a severe kind.

Owing to the greater rapidity of elimination of antitoxin when administered by the intramuscular route, Armand-Delille recommends that intramuscular injection should be supplemented the following day by subcutaneous injection of antitoxin in sufficiently large doses.

Alluding to the objection made by opponents of his method that the favourable results were due to his having used serum from horses which had formerly supplied antitoxin (vide *Medical Science*, 1919, **1**, 156), Bingel states that he had had the serum examined for its antitoxin content, with the result that the serum supplied him by one firm was entirely free from antitoxin, and that supplied by another contained only a negligible quantity (3 units in 1 c.c.). He adds that he has made no experiments as to the prophylactic action of diphtheria antitoxin, the value of which he has no reason to doubt. He also declares that he has never disputed the therapeutical value of antitoxin, but has merely seen no difference between its therapeutical results and those of normal serum.

Herzfeld, from his experience at the Leipzig University Medical Clinic, found that the use of ordinary horse serum had the following disadvantages: (1) The deposit in the throat persisted longer. (2) Paralyses were relatively frequent even after mild faucial diphtheria. (3) Cases of cardiac death, especially in adults, were more frequent. (4) An extension of the local process in the throat was more frequent than after employment of antitoxin. (5) Secondary laryngeal diphtheria could not be prevented with certainty. Herzfeld concludes that ordinary horse serum should be used only in the mildest cases in adults, which, as Feer remarks, can be treated without serum. In faucial diphtheria of any severity and in laryngeal diphtheria the use of antitoxin is imperative.

Birk states that a severe epidemic of diphtheria in Kiel, during the winter of 1918, gave him an opportunity for testing Bingel's claims. He found that cases sent to hospital wrongly certified to be suffering from diphtheria and injected with ordinary horse serum subsequently contracted diphtheria after admission to a diphtheria ward, an occurrence quite unknown when antitoxin had been given in cases of mistaken diagnosis. Birk therefore concludes that ordinary horse serum does not possess any immunizing properties.

H. Meyer, assistant at the Greifswald University Children's Clinic, injected 17 cases of mild faucial, nasal, and laryngeal diphtheria with ordinary horse serum, using $\frac{1}{2}$–10 c.c., an amount corresponding to 1,000–4,000 units of antitoxin. In three children, who had had a positive nasal culture for weeks, but had shown no other signs of nasal diphtheria, the treatment had no effect. Four cases which showed no improvement after ordinary serum, and in one case distinct spread of the membrane, were given antitoxin, when immediate improvement occurred. On the other hand, one case had a relapse after antitoxin which promptly subsided after injection of ordinary horse serum, and in the remaining nine cases ordinary horse serum seemed effective. They were, however, all mild cases which might have recovered without serum at all. Meyer concludes that ordinary serum has a certain curative action due to its foreign protein content, but by no means comparable to that of antitoxin.

P. Aaser, Superintendent of the Ullevaal Fever Hospital for 25 years, has carried out, with the support of the Nansen Fund, a long series of investigations on guinea-pigs with a view to controlling Bingel's figures and conclusions. Owing to a comparative shortage of guinea-pigs, and in order to check accurately the effect of normal and diphtheria serum, intra- instead of sub-cutaneous injections of diphtheria toxin were given, according to the method devised by Schick for the titration of diphtheria antitoxin. It was found that the amount of toxin required to provoke necrosis of the skin at the site of injection was strikingly constant; doses less than this amount gave rise either to no reaction or only to a pink infiltration of the skin. As the necrosis could be easily detected, the injected toxin was limited to the amount required to provoke necrosis. The toxin used had been stored since 1906 and belonged to the stock used for the titration of diphtheria serum.

As Aaser's tables show, an intracutaneous injection of an emulsion of diphtheria bacilli induced a reaction which, within 24 hours, was indicative of incipient necrosis (anaemia of the centre of the infiltrated area). After 42 hours complete necrosis was established. Practically the same reaction occurred when 0·2 c.c. of normal horse serum was added to the emulsion of diphtheria bacilli, the only marked effect of this addition being the delay of the necrosis by about 24 hours. Only in a few cases in which very large doses of normal serum were added, was the necrotic action of the emulsion inhibited. But when an equal quantity of diphtheria serum was added to the emulsion there was hardly any reaction after 24 hours, and there was no necrosis. Complement fixation tests also showed that no specific amboceptors were demonstrable in normal serum.

Aaser suggests that Bingel obtained no better results with specific than with non-specific serum because his dosage in both cases was far too timid. Bingel's average mortality was about 10 per cent., and in 1913 it was even 13·1 per cent. The mortality from diphtheria in Christiania in the period 1895–1919 was about 5 per cent., and during the last six years it was only 3·08 per cent., although there were many severe cases, and the disease was classified as diphtheria only when it gave rise to clinical symptoms. Aaser expresses amazement over Bingel's dosage; of the cases terminating fatally within 30 hours of admission, several received only 2,000 or 3,000 units, and only in one such case were as many as 10,000 units given. One child with descending diphtheria was given only 1,000 units. In another case of gangrenous diphtheria, admitted on the second day, and terminating fatally on the fourth day, only 5,000 units were given. Bingel appears also seldom to have repeated an injection. The frequency with which Bingel's patients developed paralysis also suggests that insufficient antitoxin was given.

Wood states that during the last six years a combined method of injecting devitalized Klebs-Loeffler bacilli and antitoxin has been used in the treatment of diphtheria by the Chicago Department of Health. If the treatment can be administered before the disease has progressed more than four days, the initial dose of the vaccine is 300 million bacilli. If the disease has lasted longer than four days, 100 million bacilli should be given, and from 3,000–5,000 units of antitoxin according to the severity of the case. The next dose may be increased to 300 million bacilli, and later to 500 million, and the antitoxin may be repeated as indicated. By this means both destruction of the bacilli and neutralization of the toxin are effected. Wood also claims that the method prevents the occurrence of carriers by destroying the bacilli in the throat. Another advantage of the method is the saving of expense in the cost of antitoxin.

Brownlie treated 50 diphtheria carriers with vaccine in doses ranging from 10 to 200 millions. The vaccine was prepared in the ordinary way and was not autogenous. One to eight injections were given. In the majority a limited number was efficacious. It was found that the vaccine produced well-defined degeneracy in the morphological appearance of the cultured organism, followed by its complete dispersal from the locality invaded. 44 of the cases which had received at most three doses were discharged with two consecutive negative cultures on the eleventh day. No bad effects were observed from the use of the vaccine.

Fraser and Duncan report three cases of diphtheria carriers successfully treated by detoxicated vaccines.

As illustrating the remarkable disinfectant properties of Dakin's solution, Haugseth records the case of a man, aged 48, who was operated on for an umbilical hernia. The wound became septic, its base necrotic, and its margins red and infiltrated. This condition did not affect the temperature or the patient's general health, but, on the other hand, it was entirely refractory to ordinary disinfectants, including hydrogen peroxide, silver nitrate, and potassium permanganate. No improvement having been effected after four weeks, irrigation with Dakin's solution was adopted with strikingly rapid effect, and the temperature, which had been about 37°, fell to 36° on the day after the institution of this treatment which was discontinued after a week. Though no bacteriological examination was made, diphtheria was diagnosed on the strength of the development of undoubted polyneuritis.

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# INJURY CAUSING SPASMODIC CONTRACTION OF SEGMENTS OF ARTERIES OF MEDIUM SIZE

The vasoconstrictor nerves supplying the wall of a medium-sized artery, such as the brachial or superficial femoral, may be irritated by blood extravasated into and around the sheath of the artery whilst the wall of the artery escapes injury, the endothelial lining of the artery is unaltered, and there is no thrombosis. But whilst the spasmodic contraction lasts there is a greatly diminished flow through the segment of the artery affected. A bullet in traversing the limb passes close by the artery, and there is induced a spasmodic contraction involving several centimetres. The spasm lasts a day more or less and then spontaneously disappears. The immediate sign consequent on the restriction of the flow of blood through the segment is the absence or marked diminution of the circulation through the limb beyond the injury. This being observed, it may reasonably be assumed that a contusion or laceration of the artery may have been produced, and that there is a danger of secondary haemorrhage and gangrene. In consequence, the surgeon proceeds to explore the artery at the site of injury; in view of the possibility of conditions to be described, it must not be hastily assumed that a contused, lacerated, and thrombosed artery exists because there is a defective circulation in the limb beyond. The condition to be described was termed by Viannay ‘La stupeur artérielle traumatique’; by Fiolle, ‘L’inhibition segmentaire des artères dans les plaies de guerre (arrêt du cours du sang au niveau d’artères traumatisées sans lésions visibles des parois ni coagulation)’; by Küttner and Baruch, ‘Der traumatische segmentäre Gefässkrampf’.

There have been numerous observations on the nerve-supply of medium-sized arteries by the sympathetic. Leriche and Heitz concluded that as soon as the sheath of the artery containing the sympathetic nerve-fibres is touched the artery enters into contraction until it has no more than one-third or one-quarter of its normal lumen in the segment involved in the contraction. Meanwhile, the artery above and below is not affected. The reaction varies in degree, being more marked in some animals, less in others. It is a reaction more evident in the brachial than in the axillary or subclavian arteries, more active in the femoral than in the iliac arteries, in the brachial even more than in the femoral.

Viannay describes the following cases:

*Case I.* A fragment of a bullet had entered the nape of the neck at the level of the 6th cervical spine and a little to the left; it had crossed the subclavian fossa and made exit through the anterior border of the axilla. There followed a large haematoma in the axilla and a loss of pulsation in all the left upper extremity. An incision was made along the free border of the pectoralis major, and next the muscle was cut across up to the clavicle. After turning out the clot the axillary artery and vein were found not to be wounded. The clavicle was then divided by excising a length of 5 cm. which exposed the subclavian artery on the first rib. It appeared uninjured but small, with a feeble pulsation, whilst there was no pulse at the wrist. The wound was sewn up with a drain, and a few hours later a pulse could be felt in the radial artery which increased until quite restored.

*Case II.* A fragment of shell passed through the back of the upper part of the arm, crossed the axilla and entered the chest. There was severe primary haemorrhage. the radial pulse was weak and irregular. Five hours after the injury the termination of the axillary and the commencement of the brachial arteries were exposed; the axillary artery pulsated well, the brachial at its commencement was very small, and the pulse in it could hardly be felt. The next day the radial pulse and circulation in the upper extremities were equal on the two sides.

*Case III.* A bullet had caused a small wound in the forearm with marked contusion, and there was no pulse at the wrist. On exposing the radial under the wound, the artery was found intact, but there was no pulsation in it for 4 cm. There was slight ecchymosis in the adventitia of the artery. The affected segment was excised, after which both ligatured ends pulsated, and there was a good recovery. No lesion could be found in the segment of the artery excised.

La Coste and Ferrier published a case in which they made observations on the blood-pressure of the injured limb. A fragment of shell had passed across the apex of Scarpa's triangle, and the pulse at the ankle below was scarcely perceptible. The superficial femoral was exposed, but found uninjured; the circulation in the injured limb had become the same on the opposite side by the second day as shown in the following table:

| | Time. | | Right. The Injured Limb. | | | Left. The Uninjured Limb. | | |
|---|---|---|---|---|---|---|---|---|
| | Hrs. | Mins. | Max. | Min. | Amplitude. | Max. | Min. | Amplitude. |
| Before operation | 14 | 30 | 13 | 10 | 1½ | 20 | 11 | 4 |
| After operation | 16 | 30 | 8 | 8 | — | 20 | 7 | 4 |
| ,, ,, | 17 | 30 | 12 | 9 | 1½ | 18 | 9 | 3 |
| ,, ,, | 20 | | 15 | 10 | 2½ | 21 | 10 | 4 |
| Next day | 7 | | 20 | 11 | 3½ | 23 | 11 | 4 |
| ,, ,, | 18 | | 21 | 11 | 4 | 22 | 11 | 4 |
| Second day | 10 | | 21 | 13 | 3 | 23 | 14 | 3 |
| ,, ,, | 18 | | 23 | 14 | 3 | 23 | 14 | 3 |

Viannay described also a case which was not the result of a bullet wound. A mechanic, whilst starting the motor of an aeroplane, was struck by a blade of the propeller on the inner side of the right arm a little above the epitrochlea. It caused a small transverse wound prolonged by a linear ecchymosis; there was little external haemorrhage. There was found a marked diminution of the radial pulse below the injury. The margins of the wound were first excised; there was then exposed a small rupture of the aponeurosis, below which the tip of the epitrochlea was bare but not fractured. On dividing the expansion of the biceps the median nerve was found intact. The sheath of the brachial artery was slightly infiltrated with blood; the artery at first sight seemed not to pulsate; on close examination a very feeble pulse was evident. On opening the sheath there was no apparent wound of the artery or of the venae comites, the wall of the artery being, perhaps, slightly more bluish than normal. The wound was sutured without a drain and healed without complication. The following observations were made on the blood-pressure:

| | Right. The Injured Limb. | | Left. The Uninjured Limb. | |
|---|---|---|---|---|
| | Max. | Min. | Max. | Min. |
| Before operation | 10 | 8 | 15 | 10 |
| 2 hours after operation | 13 | 9 | 13 | 9 |
| 16 ,, ,, ,, | 9 | 7 | 13 | 9 |
| 18 ,, ,, ,, | 9 | 6 | 11 | 7 |

Within the next day or two the maxima became definitely equal, but the minima remained unequal until the fourth day.

Fiolle's case furnishes an instance of the importance of distinguishing the condition. In a man aged 21 the bullet entered by the left buttock, crossed Scarpa's triangle and lodged in the scrotum. There was found a large haematoma in the triangle, over which the skin was violet and tense; there was no pulsation, neither in the triangle nor in the limb below. A free incision was made, which exposed the common femoral artery as it emerged from under Poupart's ligament, and the loop of a ligature was passed under it. Then the haematoma was incised and the clot turned out; also a wounded vein was ligatured. The bullet had crossed the commencement of the superficial femoral artery; the common femoral above pulsated well and was of full size; the superficial femoral appeared very small, there was no pulsation in it, it was supposed to be thrombosed. Thereupon 3 cm. of the commencement of the superficial femoral was cut out; the excised segment exhibited no thrombosis, or injury to the inner or outer coat. Profuse suppuration followed in the wound; on the 7th day there was severe secondary haemorrhage from the common femoral artery, and a ligature was applied just above the sloughing opening and below Poupart's ligament. The next day further haemorrhage was followed by death, when suppuration and sloughing were found to have extended to the external iliac artery.

In Kroh's first case of a revolver shot in the groin there was no pulse in the superficial femoral artery. The saphena vein had been cut across at its junction with the femoral. The superficial femoral artery, when first found, seemed reduced to the size of a packing-needle. After exposing 5 cm. of the artery, dividing the sheath, which was infiltrated by blood, and watching it for five minutes, it was seen to gradually enlarge and pulsate more strongly, next the popliteal artery began to beat, and a pulse was felt in the internal plantar artery.

In a second case, in which a bullet had crossed the artery in Scarpa's triangle, there was no pulsation in the popliteal artery or in the arteries of the foot, and the skin of the limb below the knee was a yellowish-white. The pulse above the site of injury and in the opposite limb was good. After nine hours the injured limb had become warm and a bright red; the arteries in the foot pulsated well. The wound healed without complications.

In a third case of a wound in the arm, following which the forearm and hand had become yellowish-white and bloodless, the brachial artery for

10 cm. above the elbow-joint was, on exposure, found to be contracted to a thread and pulseless, whilst above it pulsated strongly. After prolonged gentle stroking with the finger the artery slowly dilated to its normal dimensions, and the forearm and hand presented the most marked arterial hyperaemia. The radial pulse afterwards became equal on the two sides and the wound healed without disturbance.

Küttner and Baruch claimed to have met with 8 cases of what they referred to as a waist-like spasm of a segment of an artery. In 6 the operation gave an opportunity for an exact observation; in the remaining 2 the clinical picture appeared definite.

*Case I.* Among other slight wounds by shell fragments one entered to the outer side of the tendo Achillis, just above the os calcis, and made exit by a larger and irregular wound between the tendo Achillis and the internal malleolus; there was only venous bleeding and no bone injury. Four hours after the injury, after excising the margins of the two wounds, the exposed posterior tibial artery was found not to pulsate, so 2·5 cm. was excised, after which both the ligatured proximal and distal ends pulsated. On examination the excised segment showed no thrombosis or injury to the intima; only at one point was the adventitia infiltrated by blood.

*Case II.* A fragment of shell entered the outer side of the left thigh about its middle and made exit on the inner side about the same level without fracturing the femur. Much blood had been lost, the limb was of a pale livid colour; there was no pulse in the dorsalis pedis and posterior tibial arteries; the man could not move the limb. Five hours later a large amount of clot was turned out; the femoral vein had been ruptured, its ends had retracted, and each bled freely before being tied. The sheath of the artery was infiltrated by blood and it did not pulsate. After the artery had been exposed for 10 cm. it was noted that a length of 2·5 cm. was contracted and at first sight pulseless; above the artery pulsated, below there was no pulsation. On more careful examination a small pulse was detected in the contracted portion. Immediately after closing the wound no pulse could be felt in the foot; after a while a pulse was felt, then it was not felt, and again the pulse returned. Three hours after the operation the pulse in both feet was normal and there were no further complications.

*Case III.* A shell fragment entered the back of the arm; the wound of exit was large, just external to the internal bicipital sulcus at the same level. A tourniquet having been applied, there was much swelling below and all the arm nerves were paralysed when the tourniquet was removed, four hours after the injury. There was then no external haemorrhage, but the radial pulse could not be felt. The brachial vein had been torn across, also the median nerve lacerated. The brachial artery for the length of 3 cm. did not at first sight seem to pulsate, but on careful observation a small pulse was found passing through the segment. The arm after the operation was somewhat livid; the pulse the next day could be felt at the wrist, but was weaker than on the uninjured side; the second day the pulses on the two sides were equal.

*Case IV.* A very similar case to the last exhibited a cold bluish arm without movement and with an absence of a radial pulse ten hours after the injury. The ruptured portion of the basilic vein was cut out; there was no injury to nerves; the appearance of the artery was the same as in Case III. Twenty-fours later the limb was warm and of a good colour, with the radial pulse equal on the two sides.

The greatest difficulty in diagnosis arises in relation to the popliteal artery

*Case V.* A machine-gun bullet entered to the inner side of the knee and made a larger wound of exit on the outer side; there was no sign of fracture or of a haematoma, but of an acute effusion into the joint. The foot and leg were cold, bluish, and quite immobile; there was no pulse in the dorsalis pedis or posterior tibial arteries. The leg was raised and wrapped up; four hours later a weak pulse was felt in the posterior tibial, but the limb was still cold and motionless. On the next day the dorsalis pedis could be felt pulsating; after 48 hours the circulation had recovered, the foot and toes could be moved, and subsequently the knee. Whilst under observation for the month following there was no sign of a haematoma or of an aneurysm.

*Case VI.* A rifle bullet traversed the thigh about its middle from the anterior aspect to the inner side behind. There was free primary haemorrhage, much swelling of the thigh, the leg and foot were cold and immobile. There was no pulse in the dorsalis pedis or posterior tibial artery. The circulation generally was weak owing to shock. The limb was elevated and wrapped up, and after the general circulation had improved the posterior tibial artery of the injured limb could be felt, the leg became warm and the toes moved. Meanwhile, the swelling of the thigh did not increase. The man was three weeks under observation, during which there were no complications and the wound healed.

*Case VII.* A fragment of shell caused a wound of entry the size of a pfennig to the outer side of the right knee-joint, and a wound of exit the size of a mark in the popliteal space. The man was picked up after ten hours and operated upon eighteen hours from the injury. The leg and foot were pale, cold, and insensitive, the foot could not be moved, the calf muscles were hard but the calf was not swollen, there was no pulse in the posterior tibial artery. An incision was made into the calf for a suspected haematoma; none was found, but as no artery spurted the limb was amputated through the knee. The popliteal artery, the vein, and both nerves were found intact, only the sheath of the artery was widely infiltrated by blood. There was no haematoma in the popliteal space.

*Case VIII* was an instance of spasm affecting the common carotid artery. A bullet had passed through the neck from the anterior border of the right sternomastoid muscle at the level of the larynx to a point three fingers' breadth to the right of the 6th cervical spine. The man walked back complaining of pain in the right side of his head and dark patches before the right eye. There was no haematoma, but a thrill could be felt and a bruit heard. The artery was exposed six hours after the injury; there was a small hole in the internal jugular vein which was closed; the common carotid artery was quite intact, but for 3 cm. it was contracted to the size of a goose-quill, through which there was a small current with a thrill. Beyond this no pulsation was felt; on the proximal side there was evident pulsation. No complications arose; a fortnight later no thrill was felt or bruit heard.

The two cases described by Frassi direct attention to the danger of stroking the contracted segment, for although it may not appear thrombosed there may still be injury to the internal coat. The stroking may then induce the formation of a clot and push it onwards, so causing gangrene. A man was shot through the popliteal space, and the limb below was pulseless.

The popliteal vein had been lacerated, the popliteal artery was intact but contracted and with a very slight pulsation, until after stroking downwards, when the pulsation returned to its full extent. But the leg went gangrenous and had to be amputated. In the second case there was an absence of pulsation in a segment of the radial artery, above which the artery pulsated well. After gentle stroking of the artery the pulsation returned in the contracted segment. Gangrene ensued, and the limb was amputated.

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## NON-TUBERCULOUS JUVENILE COXALGIA

Before the use of X-rays for diagnosis, all pain in the hip of young people was presumed to be tuberculous in nature, even what were popularly called 'growing pains'. By the aid of the X-rays changes at the epiphysis, the separation of the head and the bending of the neck, producing the deformity of coxa vara were distinguished. In June 1909, A. T. Legg described to the American Orthopoedic Society, 5 cases of what he termed 'an obscure affection of the hip-joint'. He appears to have differentiated the cases from tuberculous disease, as there was no tendency to caries, caseation, and suppuration, but he did not sharply separate them from the epiphyseal changes for the recognition of which the use of the X-rays are essential, and which are in many cases, associated with rickets, early or late. Legg's cases were between 5–8 years of age, lameness had followed slight injury, resulting in thickening of the neck of the femur with little or no pain, no constitutional symptoms, little or no spasm of muscles, and no shortening.

Coxalgia being generally understood to refer to an early stage of tuberculous hip-joint disease, the term pseudocoxalgia has been adopted by some to denote the non-tuberculous disease.

In 1910, Calvé, among 500 cases at Berck, distinguished 10 cases of chronic or subacute arthritis of the hip-joint, of short duration, recovering with a mobile joint. The cases were fully distinguished by means of X-rays; the skiagrams reproduced tended to show that the changes from the normal commenced in the nucleus of ossification of the head. The normal condition of the ossifying head is that of a hemisphere, slightly concave towards the neck from which it appears separated by a translucent line. In the cases referred to it was found changed to a flattened cap, the epiphyseal line irregular, and the neck of the femur thickened. In young children the nucleus of ossification appeared subdivided, the particles later fusing to form a flattened head. But there was an absence of erosion of cartilage or bone.

An appropriate comparison may be made between Calvé's communication and that from the same hospital at Berck 10 years later by Sorrel. Using the term 'Infantile deforming osteochondritis of the upper epiphysis of the femur', Sorrel distinguished 6 among 1,500 children with hip-joint disease, in which the following changes were noted by the X-rays. In the very young the nucleus of ossification of the head appears divided into two or three unequal bits. The head resembles a flat cap. As the separate parts fuse together, the head tends to mushroom out; its process of ossification is irregular, opaque zones are intermingled with translucent areas. The epiphyseal cartilage is irregularly indented, or divided by irregular calcification. The articular line as seen in the radiographs is increased; Sorrel attributed this to distension of the capsule by fluid. The overhanging curve of the acetabulum presented in some cases irregularities, but he attributed little importance to this point. Sorrel also included changes in the neck of the femur giving rise to slight degrees of coxa vara or coxa valga.

The report on Sorrel's communication by Mouchet and the discussion on it by Lapointe and Mauclaire whilst clearly distinguishing the cases from tuberculous disease, appear to draw no sharp distinction between the changes commencing in the nucleus of ossification of the head and those at the epiphyseal line, causing deformity of the neck.

Fairbank's description of a case follows that by Calvé, and he uses the terms Pseudocoxalgia—Osteochondritis deformans juvenilis, i.e. non-tuberculous pain in the hip-joint in which the head of the femur becomes deformed owing to disturbance in the nucleus of ossification.

Perthes, in 1910, described the affection under the name of arthritis deformans juvenilis, the change being regarded as similar in its commencement to the osteoarthritis of the hip of old people, a *malum coxae juvenile* resembling *malum coxae senile,* but only advancing a little way and then undergoing spontaneous arrest.

Four illustrations from the post-mortem examination of a case by Pommer are reproduced by Kreuter. In this instance there was found a fibrillation and erosion of the articular cartilage covering the head, which had commenced just above the insertion of the ligamentum teres. Also similar changes had occurred on the opposing surface of the acetabulum. From this point of view the pathological changes of the articular surface stop short at a flattening of the head and a widening of the acetabulum and do not advance to a porcellaneous condensation of the exposed bone, or to osteophytic formations at the margins of the acetabulum.

Sundt's monograph deals with every aspect of the disease. The term 'Osteochondritis' is rejected because there appears to be no inflammatory element in the disease, and the cumbersomeness of the term Calvé-Legg-Perthes is minimized by the contraction C. L. P. Sundt's material consisted of 66 cases, most being sent to the Fredriksvern Coast Hospital for scrofula with the diagnosis of tuberculosis of the hip. A large section of the monograph is, accordingly, devoted to the differential diagnosis of these two conditions, and Sundt is driven to admit that, apart from abscess formation and other signs of destructive processes pointing unmistakably to tuberculosis, there is no one pathognomonic sign which by itself can distinguish one disease from the other. It is, therefore, not surprising to find that many of his cases were treated by immobilization for a considerable period before the non-tuberculous character of the disease was established. This, by the way, appears to be an error in the right direction, for Sundt has come to the conclusion that it is a far more serious mistake to diagnose and treat tuberculosis of the hip as a case of C. L. P. than *vice versa.*

Sundt finds that heredity, trauma, sex (male) and age (childhood) play important parts in the aetiology of this disease, whereas syphilis and tuberculosis are not contributory factors. In 110 cases of C. L. P. in which v. Pirquet's reaction has been recorded, only 37 gave a positive reaction. With regard to treatment, Sundt has come to the conclusion that the less these patients are interfered with the better. He justifies this attitude by the results of classifying his cases according as they were treated for long periods or for short spells by immobilization, or not treated at all. In 19 of his cases the limb was immobilized as for tuberculosis for a period of 1 to 4 years. In another series of 16 cases, relief of pressure on the hip or absolute immobilization was maintained for an average period of 6 to 7 months. In the last series of 23 cases observed for periods of 9 months to 12 years, the principle was adopted of letting the child run freely about and abstaining from every interference. A comparison of the ultimate results showed no differences in these three series to indicate that progress of the disease could be arrested by treatment or, on the other hand, that its course could be favoured by giving the child perfect freedom. Sundt is convinced that C. L. P. is an exceedingly common disease in childhood, that abortive forms occur frequently, and that many a case of transient limping in childhood may subsequently be proved to be a case of C. L. P. as shown by skiagrams taken in adult life.

From the numerous references to this obscure affection which have appeared of late, it would seem that injury, even slight injury, has only been noted in a few and, besides, the affection has often been bilateral; it has been described as following the reduction of a congenital dislocation, but it has also been seen on the opposite side to a unilateral congenital dislocation. One might interpret that observation as showing a congenital cause, but it is also possible to attribute it to the extra stress thrown on the sound side by the unilateral dislocation. A mild infection has also preceded the trouble.

The provisional conclusion on this obscure affection of the hip-joint would seem to be that it occurs particularly in the class of children specially liable to tuberculous disease; that it is best treated for a while in the same way as early tuberculous disease until by repeated X-ray examinations this latter assumption can be disproved, when the child should be let run about under observation. Granted the correctness of the diagnosis, it may be expected to make a complete recovery.

Such complete recoveries would seem to be the rule when the probable underlying cause, malnutrition, is at the same time overcome by good food and fresh air. But when the changes on the articular surface have been probably secondary, whether to rickety disturbance at the epiphyseal line resulting in coxa vara, or when occurring on the opposite side to a unilateral congenital dislocation, or when preceded by some infection, then there may well be permanent limitations of movement.

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C. L.

## ANTERIOR DISLOCATION AT THE ELBOW

There has been doubt as to the occurrence of an anterior dislocation at the elbow. Until the observation in 1914, by Theodore Kocher of a case at the Surgical Klinik in Bern, and a second case of the kind by his son in 1916, no previous assertion has received confirmation by X-ray examination.

*Case I.* A man, aged 40, was carrying a box weighing 25 kilos upstairs upon his right shoulder, the right arm flexed at the elbow supporting the box on that side, and his left hand on the other side. The box struck against a low ceiling, and he fell on his knee; as he got up the box slipped off his shoulder to the right, backwards; this forcibly extended his right arm, and twisted it outwards at the elbow. The pain thus caused made him fall to the ground with the box on the extended elbow. Some hours later he was examined, when the forearm was found fixed at a right angle with the humerus, abducted, and semipronated. The lower end of the humerus, including the external condyle, capitellum, and trochlea, but not the internal epicondyle, could be felt behind. In front could be felt the olecranon with the sigmoid notch and coronoid process; external to this was the head of the radius in normal relation with the ulna.

The tense biceps and brachialis anticus were partly ruptured, also the triceps. X-ray photographs showed the ulna and radius dislocated in front of the humerus, the head of the radius being displaced upward 1·5 cm., and the olecranon process 4·5 cm. The internal epicondyle had been fractured and displaced in front of, and internal to the coronoid process of the ulna. 26 years before, at the age of 14, the patient had fallen on the elbow and broken off a bit of bone, possibly the internal epicondyle. Attempts at reduction failed until, when the man was fully anaesthetized, the forearm, flexed to a right angle at the elbow, was pushed backwards and towards the inner side so that the olecranon passed under the inner condyle and was then pressed outwards into place, the radius following.

The patient recovered use of the arm, but could not completely extend or flex the elbow, being prevented by the detached internal epicondyle which he refused to have excised.

*Case II.* A man, aged 21, fell 7 metres down through an opening in a hay loft upon his left side, and in doing so struck his left elbow against the edge of the opening. He sustained, together with a fracture of the ilium, a dislocation forwards at the elbow, combined with a fracture of the olecranon. When examined the elbow was much swollen, the forearm fixed at an angle of 120° with the arm, midway between pronation and supination. The whole limb seemed shortened and the forearm displaced a little outwards. There could be felt the tip of the olecranon in its normal position with a sharp edge, also the head of the radius could be felt in front of the external condyle. The X-ray photograph showed a displacement of the ulna and radius in front of the humerus and somewhat outwards, except for the tip of the olecranon remaining attached to the triceps. The dislocation was reduced under general anaesthesia by forcibly flexing the forearm on the arm and pushing backwards, and by exerting direct pressure upon the head of the humerus.

Among some 25 cases in which this accident is said to have occurred, that published by Richet in 1839, had additional evidence supplied by a post-mortem examination. A man, aged 18, fell 14 metres from a scaffold and apparently sustained an injury to the elbow the same as in Case II above. Reduction (needless to note without a general anaesthetic) was made by extension on the forearm and counter-extension on the arm, then sharp flexion and pushing the forearm backwards. The displacement tended to recur and the elbow was fixed by plaster. Death followed from other injuries, when the brachialis anticus and the muscles arising from the internal condyle were found ruptured, the internal lateral ligament torn, and the olecranon fractured obliquely.

A. Kocher concludes that the dislocation is due to torsion so that the external or internal lateral ligament is ruptured, and the forearm screwed round the external or internal condyle whilst fully or over-extended at the elbow. Then the internal or external lateral ligament gives way, or the internal epicondyle is torn off. In the more severe cases there is a fracture of the olecranon process; in that case the dislocation forwards could occur in acute flexion.

In connexion both with dislocations and fractures at the elbow, Kirmisson recalls Malgaigné's view that the common dislocation backwards at the elbow occurs in extension, or with only slight flexion, combined with torsion.

There is thus agreement as to the importance of torsion in both instances, in the case of the very rare, as in that of the common dislocation.

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## THE PHYSIOLOGY OF PAIN

Pain is so common, in fact so universal an experience, that it is apt to be taken very much for granted and to escape any very searching curiosity as to its ultimate significance.

It is of course true that philosophy has always been much occupied with the problem of pain, but such inquiries have mostly been conducted upon an assumption, whether acknowledged or not, which makes their value to the biologist almost negligible.

The object of practically all philosophic speculation has been to demonstrate some kind of congruity between man's moral nature and the universe at large. The subject of pain, therefore, has been approached by the philosopher under the conviction that the phenomenon must necessarily and however indirectly have value and meaning for mankind. In consequence, we see ascribed to pain a 'disciplinary' function in human experience which enables the philosopher to regard it as a not inconsistent element in an anthropocentrically constructed universe. Such methods and conclusions are, however, very unsatisfying to the biologist who is met at the outset by the fact, so very evident to objective examination, of the enormous discrepancy between the amount of experienced pain in the world and any observed physical, mental, or moral benefit that ensues to the sufferers.

Other methods must be used if results capable of resisting criticism are to be attained, and it was to these objective modes of inquiry that we were referring when we suggested that the general significance of pain as a biological phenomenon had attracted relatively little curiosity.

It is perhaps commonly assumed that pain is to be regarded as an evidence of disturbance of function similar in its general features to other such manifestations, and strictly comparable, for example in a broad way, with vertigo, vomiting, wasting, paralysis, and so forth. It is assumed, that is to say, to be related as to its origin and continuance with some definite underlying abnormality of which it is a more or less precise expression and measure. The further assumption is also not infrequently made that in a general way pain may be looked upon as having a distinct though perhaps indirect functional meaning and value to the individual, so that within limits sensitiveness and liability to pain constitute conditions tending to favour survival.

Consideration, however, shows that these assumptions cannot be accepted without great reservations, and that pain as a symptom occupies a position by no means strictly analogous with that, for example, of dyspnoea or vomiting. Certain peculiarities in the status of pain are not difficult to detect and they may be indicated in three broadly definable groups. Of these groups the first is concerned with the frequency of pain, the second with the relations between pain and its pathological causes, and the third with the functional value of pain to the individual.

**The frequency of pain.**—Pain is undoubtedly by far the commonest disturbance of well-being to which man is subject. Not only is it the almost universal manifestation of well-defined injury and disease, but it spreads its range much farther into experience than this. If one watches oneself carefully, even the healthiest will find that quite apart from injury he rarely gets through a whole day without some experience of bodily pain, some usually transient twinge or stab or ache that easily lapses from a healthy memory because it is unaccompanied by any other evidence of abnormality.

**The relation of pain to its bodily cause.**—It is a commonplace of practical medicine that pain is of all symptoms the one most likely to show itself persistent and inveterate, and it is perhaps true to say that the more pain is a predominant symptom the more difficult it is to treat effectually. The longer the time during which pain has been experienced the more difficult it is to relieve, though the originating lesion has ceased to progress or even been eliminated. It may even be said that when severe pain has been present for a long time, it seems as it were to become ingrained in the very substance of the nervous system, and to have become truly ineradicable.

**The functional value of pain.**—Within the comparatively narrow limits of recoverable injury, pain undoubtedly has a value for the individual and furnishes unmistakable guidance whereby the life or the activity of the patient may be preserved. The value of sensibility to pain in this regard is very well illustrated by the diseases such as tabes and syringomyelia, in which analgesia of the limbs is a usual symptom. There can be little doubt that the so-called neuropathic arthritis of these conditions is due to persistent use of joints under circumstances of slight injury, when in the normal subject pain would have rendered disuse and rest imperative.

When we consider the usefulness of pain to the individual and to the species, it soon becomes obvious that a distinction must be sharply drawn between pain in relation to disease and pain in relation to injury. In disease pain is almost wholly without usefulness to the sufferer. Apart from a few exceptional cases, such as perhaps the pain of acute pleurisy and of caries of the spine, pain is no more than an arbitrary and superadded affliction. It is difficult to suppose that the pain of cerebral tumour, of renal or biliary colic, of cancer, of trigeminal neuralgia, has the slightest functional value to the patient. Moreover, in most cases of cancer pain is characteristically absent in the earlier stages, and present only at a period when successful treatment is doubtful or impossible. Again, certain diseases consist, as it were, entirely of pain; in trigeminal neuralgia, and the pain that sometimes follows amputation, the one symptom constitutes the whole disease and may continue for twenty, thirty, or even, as in one case known to me, sixty years. Such cases constitute the very acme of the functional uselessness of pain. A superficial examination then of pain as met with in practical medicine furnishes a fair body of evidence that its position as a symptom is remarkable, even perhaps unique. Let us now turn to what we know of the mechanism of pain in the normal.

**Sensibility to pain in the skin.**—It is in the skin that the mechanisms of sensibility to pain most easily lend themselves to physiological study and it is upon work done in this field that most of the facts available are based.

It will be convenient to enumerate first certain facts which have been established as the result of work done on the normal and normally innervated skin by a large number of workers, chief amongst whom, by general consent, is v. Frey.

(1) Sensibility to pain in the skin has, like tactile and thermal sensibility, a punctate distribution. Pain spots react to painful stimuli alone, just as tactile and thermal spots react to the corresponding stimuli alone, provided the stimulus in a given case does not pass outside the appropriate spot.

(2) While the adequate stimulus to a touch spot is mechanical (or electrical) alone, and the adequate stimulus to a thermal spot (heat or cold) is thermal alone, the adequate stimulus to a pain spot is mechanical, electrical, or thermal (heat or cold).

(3) At the same time, however, the mechanical stimulus that would excite a touch spot has to be increased in intensity in order to stimulate a pain spot, and the same applies to thermal stimuli. That is to say, the threshold of the pain spots is relatively high for the same stimuli as compared with the touch and thermal spots.

(4) The quality of the sensation 'pain' is characteristically different from all other sensations in being urgent, in tending to some kind of compulsory motor reaction, and in being charged with affective quality.

(5) The cornea possesses sensibility to pain alone, and in it the only nerve-fibres present terminate in free arborizations among the cells. It is therefore assumed that the *free naked arborization* is the end organ of nerve-fibres giving sensibility to pain.

Thus far then we are able to make the important general statements that the peripheral pain mechanism is *excitable by a number of different stimuli which have no single physical character in common*, that while it *requires a stimulus relatively intense, it yields a reaction relatively excessive*, and that *its characteristic anatomical feature differs strongly from all other so-called end organs* in being a mere free and naked terminal arborization.

It is necessary to give particular attention to the accessibility of the pain mechanism to a number of different stimuli. Of the other specific sensory spots in the skin each is accessible to one stimulus alone which represents a simple unanalysable physical process—the touch spot responds to movement, the heat spot to transference of heat to the skin, the cold spot to transference of heat from the skin. The *pain spot is accessible to stimulation by all these, and hence* the mechanism is destitute of that adaptation to registering a single physical change which is characteristic of all other peripheral mechanisms, including those of the special senses. The only unitary feature in the stimuli of pain is that they are such that a moderate increase in their intensity (with the exception of electrical stimulation) would inflict actual damage. It is suggested in explanation of this apparent anomaly that in the process of natural selection the skin has acquired what Sherrington calls a 'specific sense of its own injuries'. It must be admitted, however, that there is a difficulty in regarding as the essence of a stimulus, not the physical characters it actually possesses, but those it would possess if it were something else. It is also suggested that the supposed absence of a specific end organ of the pain nerve is in accordance with its high threshold and its accessibility to various stimuli, for the specialized end organ is regarded as at the same time increasing accessibility to one specific stimulus, and diminishing it to all others.

Supposing these views to be accepted, they still give us no special insight into the physiological meaning of the excessive reaction and unpleasant affective tone so characteristic of the pain sensation.

When we consider the number of simple sensations which in isolation are almost altogether free of urgency and affective tone, the extent to which these accompany the smallest and most elementary experience of pain cannot fail to seem remarkable and to be a peculiarity, the explanation of which should lead us into the inmost significance of the pain mechanism. Simple touch, heat and cold may at times be accompanied by a certain amount of affective tone; for example, some degrees of warmth are exceedingly pleasant, but they have no element whatever of urgency and tend to produce no impulse towards motor reaction. It seems therefore probable that the urgency of pain is not an ordinary sensory quality that enables us to recognize the stimulus, but something superadded and belonging to the nature of the pain mechanism. The sensation 'touch' is easily evoked, and as it were flows quietly and smoothly into the sensorium, its sole effect being to inform the subject of a simple movement at the periphery; the sensation 'pain' is more difficult to evoke, but when its threshold is reached seems suddenly to burst upon the sensorium, liberating at the same time a veritable explosion of reactive energy.

Now it happens that we possess other evidence that the urgent element in pain is not what we may call a mere 'recognition quality,' is not, that is to say, merely the means by which we recognize a stimulus likely to become injurious. In animals and man, after division of the spinal cord, different reflexes are elicited by stimulation of the lower limb according to the nature of the stimulus. The response to a stimulus that would cause pain in the intact animal, is a vigorous widespread and defensive movement; the response to a stimulus that would not cause pain in the intact animal is a totally different movement which will frequently, for example, have a postural adaptation. Moreover, the response to the 'pain' stimulus is prepotent over other responses, and if the two stimuli are applied simultaneously or successively, the former will anticipate or interrupt the latter as the case may be.

The study of pain in the normally innervated skin furnishes us, then, with a large body of evidence that it is in certain respects unique among all the other forms of sensibility, and gives us a reason to suppose that the mechanism which subserves it can be understood only upon principles perhaps fundamentally different from those in accordance with which the other peripheral mechanisms manifest their function.

**The results of experimental nerve section in man.**—In 1905 papers were published by Dr. Head giving the results of a wholly new method of investigating the sensibility of the skin—the method, that is to say, of experimental section of cutaneous nerves in man. In 1909 and 1913 observations founded on the use of the same method were published by Trotter and Morriston Davies. More recently (1916) Boring in America has published a contribution to the same subject also based on the method of experimental nerve section.

There can be no doubt that the new mode of attack on the problems of cutaneous sensibility has yielded a body of precisely established facts which could have been discovered in no other way. The method, however, is so laborious that in fifteen years it has been used by only three groups of investigators. It is therefore natural that no exact agreement upon the whole body of observations has been reached, and that the theoretical conclusions arrived at by the different groups of inquiries has been widely different. The reviewer does not propose to attempt here any critical examination of these three contributions to the subject, but will merely try to define what new material has been obtained which bears upon the physiology of pain.

Numerous as are the differences and discrepancies of detail, there emerges from the whole series of observations the broad fact that during recovery of a sensory nerve after suture there is a tendency for the characteristic features of sensibility to pain to be greatly exaggerated, and for other forms of sensibility to take on similar characters to a greater or less extent. The sensation of pain elicited from the recovering area is extraordinarily intense, explosive, and unpleasant, and causes a practically uncontrollable impulse to some motor response. The sensation of cold assumes similar characters to a remarkable extent; it becomes urgent, explosive, extraordinarily intense, and associated with painful stinging. The tendency to a motor response is strong, the affective tone unpleasant, and the sensation distractingly vivid and obsessing.

Traces of a similar kind of intensification are to be met with in recovering sensibility to heat and to touch, but in neither case are the phenomena so striking as they are with pain and cold. There are reasons for supposing that this is due rather to intensification being necessarily less conspicuous with manifestations of these forms of sensibility than to the tendency to the production of it being less pronounced. For example, the intensification of heat very easily produces a sensation of pain in which the thermal element is very difficult to distinguish.

That all sensations in a recovering area tend to undergo what we have called intensification is, within limits, generally admitted by all workers in this field. That this intensification represents a modification of all types of sensibility towards the type which in the normal is shown exclusively by sensibility to pain is an interpretation shared in neither by Head nor by Boring, who explain the phenomenon by hypotheses far more elaborate. Both of these observers proceed upon the assumption that any peculiarities of sensibility shown in recovering areas must be explicable in terms of defect only, and are the result merely of some function having not yet returned. It was pointed out by Trotter and Morriston Davies that the events which accompany and follow section and suture of a nerve constitute a pathological process, the existence of which makes it necessary to consider as a causative factor in the ensuing sensory peculiarities the possibility of a *disturbance* of function as well as a *defect* of function.

What are the processes which follow upon a nerve section and suture? The very familiar histology of these changes need merely be summarized here in the briefest way.

*Below the Section:*

(*a*) Degeneration and disappearance of axis cylinders.

(*b*) Proliferation of the neurilemma sheath so that its lumen comes to be occupied by a solid column of cells.

*At the Section:*

(*a*) Ramification and outgrowth of axis cylinders from the central end, some finding their way into the peripheral end; others escaping into the tissues about the suture line and wandering irregularly there. There is apparently nothing which attracts the axons to the peripheral end toward which their course is always irregular and wandering.

(*b*) Fibrosis of the tissues in and about the suture line apparently excited by the presence of the naked axis cylinders, which appear to be irritants of connective tissue proliferation.

Similar changes are seen after simple division of a nerve, as in an amputation. The so-called amputation neuroma or bulbous nerve end is chiefly made up of very numerous axis cylinders which have issued from the central end in a veritable spray. These are found pursuing a complicated convoluted course embedded in an extremely dense connective tissue.

The study of such conditions gives one the strongest impression that when a nerve is cut across and left free, there is a pronounced antagonism between the escaping nerve-fibres and the surrounding connective tissues. The nervous elements seem to seek to invade, the connective tissue elements to restrict the invasion, and each seems to be excited to activity by the other. The changes found about the line of a satisfactory nerve suture are of the same kind, but naturally of less degree, as many of the outgrowing axons are received by the waiting and approximated peripheral end. There is evidence then at least to suggest that the regeneration of a nerve is not a process that occurs wholly as a matter of course, but rather that it is to a certain extent resisted and precarious. Moreover, it would appear that the downgrowing axis cylinders are exposed to irritative influences, and that those which fail to find the peripheral end of the nerve must be particularly liable to this. Clinical experience of nerve suture in man leaves no doubt at any rate of the fact that regeneration is never certain and frequently incomplete.

We may ask next whether there is any collateral evidence of the existence of this apparent hostility or incompatibility between the neural and somatic tissues.

**The insulation of the nervous system.**—When we consider the anatomy of the central nervous system we cannot fail to be struck by the number and complexity of the mechanisms the apparent function of which is to insulate the nervous tissues from contact with the somatic, except at certain restricted points where regulated contact is necessary for function.

The dura mater is commonly regarded as functioning chiefly as a mechanical support. This view scarcely accounts for the dural lining of the skull and the dural sheaths of nerves, for the extreme density and imperviousness of its substance and for the fact that of all membranes of the body it is the one most certainly and rapidly reformed after excision of part of it. If one excises a part of the dura at an operation, and has to expose the parts again at a subsequent operation in a few weeks, one invariably finds the dura completely restored and scarcely distinguishable from the normal, even though at the first operation one has laid the raw surface of the scalp flap upon the bare brain. The new dura always possesses the three characteristic features of the normal membrane—a glistening inner surface, extreme density of substance and differentiation from the overlying parts, so that the scalp readily strips off it.

Another similar evidence of this neurosomatic incompatibility is afforded by the established fact that it is impossible permanently to drain the cerebrospinal fluid into any somatic tissue or cavity. The cerebrospinal fluid apparently shares in the physico-chemical characters of neural tissues, for wherever it is allowed to escape into the subcutaneous tissues, peritoneal cavity or so forth, a cyst wall forms about it having all the characters of a dura. The supply of the central nervous system with vessels, and the necessary somatic intrusion this involves, is met by every vessel that penetrates the nervous substance being insulated by the so-called perivascular lymphatic—a structure otherwise very difficult to account for.

Again, it cannot be regarded as physiologically insignificant that ordinary connective tissue is practically excluded from the structural support of the central nervous system, while the skeletal properties which are peculiarly necessary in the brain and spinal cord are supplied by a special tissue of neural origin, and therefore, unlike all the mesoblastic tissues of the body inert towards nerve protoplasm.

Pathological illustrations of the same fundamental principle are numerous and striking. The glioma, although behaving in the brain like a malignant tumour, never infiltrates the dura or invades the skull—it is essentially a neural neoplasm. Endothelioma of the dura which infiltrates the skull and behaves like a malignant tumour there, does not infiltrate the brain and remains separable therefrom though deeply embedded in it—it is essentially a somatic neoplasm.

An excellent illustration of the seclusion of the central nervous system from the body is the impenetrability of the neural tissues to certain drugs—as is shown, for example, by the resistance of the parenchymatous infection of general paralysis to antisyphilitic treatment, while the connective tissue and truly extraneural gumma of the brain responds.

**The insulation of the peripheral nerves.**—The peripheral nerves from the very nature of their function cannot be protected from contacts which would produce reaction by a general seclusion such as is satisfactory in the case of the central nervous system. Each individual fibre must therefore be insulated by a special envelope which need not be present around fibres contained in the spinal cord and brain. The neurilemma seems to fulfil these requirements. It is absent or rudimentary in the brain and cord, where the nerve can meet only such tissues as are to it physiologically inert, but it is present throughout the whole peripheral course of the nerve. Provided with this sheath a nerve-fibre can traverse any part of the body and remain inert to all the tissues with which it comes into relation, until it reaches the structure with which it is functionally related.

Though not strictly relevant, it may be interesting to note that if, as has already been hinted, the outgrowth of new nerve-fibres during regeneration is the result of the stimulating effect of contact with the somatic tissues, the absence of regeneration in the spinal cord may be due to the absence of any such excitant contact. Absence of neurilemma and absence of regeneration within the central nervous system would not then be cause and effect as sometimes supposed, but both effects of the same thing—complete physiological seclusion.

When we see neurosomatic contact so carefully guarded against in the whole structure of the nervous system, we may reasonably suppose that the contact that is made even in the most careful section and suture of a nerve, is not without serious effects. That such effects on the side of the nerve are in the nature of a continuous excitation is shown by the results of the division of nerves in amputation. In every such case the patient's consciousness of the lost limb is increased rather than diminished by the operation. He is acutely and more or less painfully aware of this phantom, and is probably receiving abundant impressions as a result of irritation of the raw nerve ends by the tissues in contact with them. In the majority of cases the phantom limb fades within a few weeks and one must assume that an equilibrium is reached between the invading efforts of the nerve-fibres and the encapsulating activity of the tissues. In some cases, however, such equilibrium is greatly delayed or never reached. The ends of the nerves continue to suffer a persistent excitation, and the patient to be plagued by a painful phantom limb.

If one is right in supposing such a phenomenon to be due to excitation of the cut nerve, we may suppose that the sensations experienced would bear some relation to the number of fibres of various kinds in the nerve. Now it is probable that sensory fibres reporting movements are those most numerous in the limb nerves, and corresponding with this is the observed fact that perhaps the commonest of all complaints by patients is that of painful cramp-like fixed postures of the phantom limb.

Having reached the position that the fibres of a regenerating nerve are probably exposed to a varying degree of continuous irritation, we have next to ask if this can be correlated with that intensification of sensibility in the recovering area which makes all forms approximate to the type which is represented in the normal by sensibility to pain.

Now we have seen that pain nerves end in naked arborizations which necessarily keep them in direct contact with non-neural tissues. May we not suppose then that the pain nerve is a nerve that is constantly exposed to a limited mild subliminal excitation and that the secret of the peculiarities of the pain sensation lies in the fact that the nerve by which it is originated is a nerve differing from all other nerves in being normally in a state of continuous excitation. This would at any rate give us a tentative explanation of the explosive quality, the unpleasant affective tone and the tendency to motor response characteristic of the experience.

**The relation of pain to other forms of sensation.**—It would follow from what we have just said that the nerves subserving tactile and thermal, that is, discriminative sensibility, differ from pain nerves in lacking this chronic excitation and in being as it were damped down. It will be remembered that all other end organs than those of pain, widely various in structure as they are, show one constant feature, and that is that the terminal nerve fibrils are shut in by a well-marked encapsulating formation. Whatever may be the function of these organs the constant recurrence in their structure of this element of encapsulation suggests that the insulation of the nerve fibril from contact with the surrounding tissues is of great importance, and the other considerations we have advanced allow us to suspect the completeness of the insulation of such nerves to be a means of damping down their general excitability so that the sensations they originate shall be without urgency and explosiveness and permit of that quite sensory atmosphere in which alone deliberation and discrimination are possible.

**Aspects of neural evolution.**—From this point of view we get perhaps a glimpse of the way in which the evolution of common sensation has proceeded.

The germ of a nervous system is a group of cells capable of irritating and being irritated by the other cells of the body. The essential hostility of neural and non-neural tissues gives us perhaps a hint of the physiological significance of the ectodermal origin of the nervous system and of its being formed at the surface and then sunk *en masse* into the substance of the embryo. If this hostility is fundamental, not less so is the need for limiting and regulating the opportunities for contact between the two tissues, which must therefore be separated by an impenetrable wall in which openings are present only at the exact spots where interaction is valuable. In many invertebrates the nervous system is a mere diffuse subcutaneous plexus, and from that state onwards in the animal scale there is an extended series of increases in the centralization and insulation of the nervous system—centralization, however it may have come about, very obviously rendering insulation easier. In discussing the insulation of the human nervous system we have seen how very elaborate and complete the mechanisms securing this condition have become.

Now in animals with a diffuse nervous system response to stimulation seems to be for the most part immediate and urgent. We may suppose that the relatively uninsulated nervous system yields in general afferent impulses of the explosive type, and that in such animals what sensation there is, is all of the quality which survives in us only as pain. Delay between stimulus and response, which is the fundamental function of a centralized nervous system, is possible when advancing insulation has damped down the urgency of incoming sensations; as soon as delay is possible deliberation and discrimination appear.

It is at any rate tempting then to regard sensibility to pain as the survival in us of the primordial mode of sensation. Its urgency and tendency to evoke immediate motor response is the reproduction of the normal experience of the lower invertebrate. From it the discriminative forms of sensibility have been differentiated by the progressive increase of insulation. Regeneration of a nerve by exposing a greatly increased number of nerve-fibres to somatic contact and irritation throws back all forms of sensibility more or less into the primitive type and provides an explanation of the characteristically variable phenomena of recovery after suture. If we view pain as an exaggerated response by a physiologically irritated nerve, it is possible to get some conception why pain is the commonest of symptoms and why it is so apt to become inveterate. Pain is, as it were, physiologically only just not present in us all, and what appears to be a very slight disturbance pathologically may prove an effective and incurable excitant of it.

**Boring, E. G.** Cutaneous sensation after nerve division. *Quart. J. Exper. Physiol.*, 1916, **10**, 1.

**Head, H., Rivers, W. H. R.**, and **Sherren, J.** The afferent nervous system from a new aspect. *Brain*, 1905, **28**, 99.

**Trotter, W.**, and **Morriston Davies, H.** (1) Experimental studies on the innervation of the skin. *J. Physiol.*, 1909, **38**, 134.

**Trotter, W.**, and **Morriston Davies, H.** (2). The peculiarities of sensibility found in cutaneous areas supplied by regenerating nerves. *J. f. Psychol. u. Neurol.* (*Ergänzungsheft*), 1913, **20**, 102.

W. T.

# ABSTRACTS

## SURGERY

**Krogius, A.** Studier och betraktelser öfver den Dupuytren'ska fingerkontrakturens patogenes. [**Studies in the genesis of Dupuytren's contraction.**] *Finska Läk-sällsk. Handl.*, 1920, **62**, 489–506.

Of the 22 cases of Dupuytren's contraction treated in the period 1888–1920 at Kirurgiska Sjukhuset in Helsingfors, 18 were males, and only 4 females. In 2 cases the age of the patient was between 10 and 19, in 6 between 20 and 29, in 4 between 30 and 39, in 4 between 40 and 49, and in 6 between 50 and 59. Thus, in more than half the total the disease began before the 40th year. The disease was bilateral in no fewer than 12 cases; in 7 it was confined to the right and in 3 to the left hand. In 4 cases there was a family history of the disease, and in one of these it had appeared in as many as 16 members of the same family distributed over 4 generations. No correlation between manual labour and the disease could be uniformly established, and several of the patients belonged to the intellectual classes. Among the 50 professors of Helsingfors, 5 exhibited this deformity.

Krogius examined microscopically 13 cases, in 2 of which the contraction had lasted only a few months. In others it had lasted for several years, in 2 for more than 20 years. He also examined microscopically the palmar aponeurosis of new-born infants, and found among the bundles of connective tissue small islands of transversely striated muscle obviously undergoing conversion into connective tissue. Among his sections of Dupuytren's contractions he could never find in the thickened palmar aponeurosis any small-celled infiltration or other sign of an inflammatory reaction. Nor could he ever in these cases encounter transversely striated muscle-fibres. He concludes that this condition is a developmental disorder of the superficial palmar muscle (flexores breves manus superficiales). Just as the palmar aponeurosis itself must be regarded as a fibrous equivalent of certain muscles of the palm in some mammals and in the human embryo, so the fibrous tissue of Dupuytren's disease may be regarded as a product of an embryonic relic of the same muscular layer. The subjects of this disease do not possess atavistic muscles in the strictest sense of the word, but they develop the disease because, imbedded in the palmar aponeurosis, there are musculo-tendinous islands which later in life develop into fibrous tissue and thus provoke the characteristic contraction. But though Krogius regards the disease primarily as one of 'embryonic tendency', he does not deny the importance of trauma in a certain proportion of cases; it may, indeed, be the determining and exciting cause. C. L.

# NEUROLOGY

**Hurst, A. F. The psychology of the special senses and their functional disorders.** *Oxford Medical Publications*, 1920.

Under the above title Dr. Hurst has published in full the Croonian Lectures delivered by him in 1920. The book is a record of the extensive observations by him and his colleagues on the action of suggestion in producing functional symptoms in normal people, and in relieving gross manifestations in hysterics. The author has shown in a very conclusive way that many physical signs usually considered to be pathognomonic of organic disease are in reality functional; and great praise is due for the thorough manner in which he has worked at this subject over a wide field. In view of the publicity which his work enjoys, it will be difficult for a practitioner to fold his hands over any kind of case and say that nothing can be done; for Dr. Hurst has shown that in every case of organic disease there is an hysterical element, and it should be the business of the doctor to disentangle this and get rid of it. This is all to the good, and may, perhaps, be a corrective to another school of thought, now enjoying an equal publicity, whose avowed aim is to register the symptoms of illness for years, it may be, before there is any disability at all.

Dr. Hurst's work is so good that one wishes that his vision were a little wider, that he could see that his dictum, 'Hysteria is a condition in which symptoms are present which have resulted from suggestion and are curable by psychotherapy,' does not cover the whole ground, and that his associated statement, that after the removal of such symptoms by psychotherapy the patients were fit and no more liable to develop new symptoms than other people, is not wholly in accordance with fact. Not only did those who worked in other hospitals see Dr. Hurst's failures from time to time, just as he tells us he saw theirs, but in this very book there are cases recorded which demonstrate that these two propositions of his are untenable.

He describes two examples of hysterical deafness, in each of which the cure of the deafness was followed by amnesia, which had not been present before. He mentions these two striking occurrences without comment, and it is clear that for him they were of little significance. One man had a complete loss of the whole epoch, some sixteen months in duration, between his enlistment and the day on which his deafness was removed. So complete was it that he had to relearn the whole of his drill when he was returned to duty. Now, are we to suppose that this amnesia was not of hysterical nature? If it was, who or what had suggested it? It was so dramatic that it is astonishing that so important a question, involving as it did the implication of faulty technique, was overlooked. Why was it not cured by psychotherapy before the poor wretch was sent back? An amnesia of sixteen immediately preceding months would be no light handicap for any one of us with which to face the world. Dr. Hurst must have considered it hysterical; he would not have sent a man back to duty with a brain lesion so gross as to have caused a symptom like this. Is it not possible that beneath the manifest symptom of deafness there was a strong, perhaps unconscious, wish to have nothing more to do with war, that when

Dr. Hurst made a return to war likely the mind reacted by dissociating all knowledge of anything that had to do with war, and that in this way the wish was fulfilled? Surely there is here an instance of a mental attitude in these patients, which it might be advisable to understand and to alter, something quite different from a symptom, but which was the cause of a symptom that did not arise from suggestion, was not curable by the psychotherapy of persuasion, but yet was an hysterical symptom.

Dr. Hurst has devoted considerable energy to the study of the so-called stigmata of hysteria; and because he has found that they, both somatic and mental, are always artifacts, he has somehow come to the conclusion that there is nothing in hysteria beyond the symptoms. It is a strange conclusion from such a premiss; for the stigmata, if they existed, could themselves be only symptoms, symptoms of a more permanent character than paralyses or contractures. Their disappearance from the scene leaves the problem untouched. Hysterical symptoms characterized by loss are explained by the psychological mechanism of inattention. Physically, this is described as being probably due to retraction of dendrites. In severe cases these remain retracted during sleep, so that the hysterically deaf do not hear even in sleep. Dr. Hurst says that he hoped to be able to cure hysterical deafness by hypnosis, and was surprised that he failed; but he found an explanation in the probability that the dendrites were retracted in hypnosis just as in sleep. This is very interesting, for it is a good example of the way in which a fanciful pathology leads astray. It is possible that, though Dr. Hurst consciously expected cure by hypnosis, his unconscious knew from the sleep analogy that he would fail, and that he therefore tried only half-heartedly and did fail. The present writer had no difficulty in curing several cases of hysterical deafness by hypnosis.

In the section of the book dealing with ocular troubles there is curiously no mention of what used to be called neurasthenic asthenopia, where the patient can read quite well for five or ten minutes and then everything gets blurred. This is probably the commonest of all functional eye troubles, much commoner than blindness or fixed accommodation difficulties. As the patient can always see clearly for some minutes, it is difficult to fit the symptom into a pathology of 'not looking'.

It must be said again that Dr. Hurst's work is of great value. The removal of hysterical symptoms is well worth while. If the patient has not to return to a difficult environment nothing more may be needed. Even if he has, it is a useful preliminary to further investigation; it makes the patient willing to co-operate. T. A. R.

**Viets, H. Relation of the form of the knee-jerk and patellar clonus to muscle tonus.** *Brain,* 1920, **43**, 269.

Viets, working in Sherrington's laboratory, has investigated the relation of muscle tone to the knee-jerk. This subject was recently reviewed in *Medical Science,* and there is little to add to what was then stated (1920, **2**, 346).

He finds that in the spinal animal the knee-jerk is a single twitch followed by rapid and complete relaxation of the muscles. There may be a single rebound jerk, or several, after relaxation.

In the decerebrate animal, or in the spinal animal, when the vasticrureus is rendered tonic by reflex stimulation, the knee-jerk is a single twitch followed by a continued contraction, the muscle assuming a new and shorter length after the jerk. There are then two elements in this jerk, the twitch or 'contractile' element, and the tonic or 'plastic' element. It is this second element that is the true index of muscle tone. It varies according to the tone of the muscle and disappears when this is reflexly inhibited.

The flaccid muscle of the spinal animal is not completely toneless, but contains an element of spinal tone, which can be reflexly inhibited. When this inhibition is complete the muscle gives no jerk.

Clonus is best obtained with a low degree of tonus, and the range of tonus through which it is obtainable is small. Beyond this range, either increase or decrease of tonus causes it to disappear. The appropriate degree of tonic shortening is called the 'neutral tension' of the muscle. A true clonus consists of a series of self-sustained twitches, regular in rate and amplitude, superimposed upon a tonic shortening. Its rate ranges from 12 to 17 per second.

It is perhaps unfortunate that the slighter degree of clonus which dies out after five or six beats is called 'pseudo-clonus' by Viets. There seems no fundamental difference between it and the stronger clonus that persists, while the specific meaning attached to the phrase by the clinician makes this use of the word misleading.

The plastic element of spasticity in man is possibly better appreciated than Viets imagines, and its occurrence has been observed and recorded. However, owing to practical difficulties in graphic registration of reflex movements in patients, to which Viets refers, there have been no adequate permanent records made.

The tendon-jerks, obtainable in man from flexor muscles, have never been examined in experimental animals. In view of the more or less selective incidence of tonus, it would have been interesting had some reflex comparable with the hamstring-jerk of man been investigated in the decerebrate and spinal animals, and its dependence upon contractile tone determined.

F. M. R. W.

**Wilson, S. A. K. On decerebrate rigidity in man and the occurrence of tonic fits.** *Brain*, 1920, **43**, 220.

Wilson describes a series of cases in which, in association with various abnormal conditions of the brain, and with or without loss of consciousness, there was observed a persistent tonic extensor rigidity of the musculature. This may be unvarying in intensity, or it may be periodically increased by the occurrence of 'tonic' or postural fits. These are the 'tetanus-like seizures' of Jackson, and they may also occur apart from persistent rigidity. Wilson regards this rigidity as strictly analogous with the decerebrate rigidity of Sherrington, while the tonic fits are in reality 'attacks of decerebration'. When the condition occurs during conscious life, it is not associated with tonic fits, and it may be localized in one or more limbs or segments of a limb. Underlying the involuntary movements of chorea and athetosis is a 'postural background which is composed of part of the complete decerebrate attitude'.

The essential feature of the lesions producing these phenomena is that they dissociate the cortex from the mesencephalo-cerebellar level, and at the same time leave the latter functionally intact.

The rigidity is the expression of a non-cortical motor mechanism which finds its full expression in decerebrate rigidity and in complete tonic fits.

The rigidity produces extension of the head, neck, and trunk, sometimes with opisthotonos, the upper limbs are fully extended and adducted with the forearms pronated and the wrists and fingers flexed. The legs are extended and adducted, the feet plantarflexed, and the toes dorsiflexed. If the two halves of the body are unequally affected the head is rotated to one side. The tonic fits are sudden in onset and cause a marked increase in the rigidity, but do not modify its form. They are associated with slowing of respiration, sometimes with Cheyne-Stokes rhythm, and dilatation of the pupils. He has observed cases in which tonic fits occurred, but in which there was no residual rigidity between the fits.

Several of the cases did not die, and therefore the site and nature of the lesion could not be accurately determined, but in such cases as came to autopsy the lesions were various—cerebral haemorrhage, meningeal inflammation, and tumours—while he also cites hysteria as a cause. In cases of athetosis and of chorea, Wilson, also on purely clinical grounds, believed that he detected partial or localized manifestations of decerebrate rigidity.

Wilson makes no reference to previous work devoted to the study of decerebrate rigidity in man, and therefore does not include the rigidity of hemiplegia and of spastic paraplegia, in which this tonic manifestation has been most definitely identified. In fact, he says, in reference to hemiplegia, 'It might be supposed, simply, that the ordinary hemiplegic attitude of arm and leg is a unilateral decerebrate posture, but this is the case only in a sense.' What this sense may be he does not add, nor is any explanation afforded of the spasticity of pyramidal tract lesions, though this might be considered to demand consideration in this connexion.

It is not certain from the clinical records that in all the cases there is evidence of the withdrawal of cortical control, which is an essential condition for the appearance of rigidity. This may be reasonably objected to the cases of chorea, while it is not very clear why pronation of the hand without any trace of underlying rigidity should be regarded as a segmental decerebrate rigidity.

It seems unfortunate, too, to complicate a fairly clear conception by the admission of the attitudes of hysterical fits. Surely these cannot be attributed wholly to a 'release mechanism', but demand something more than an uncontrolled normal activity of the midbrain postural centres for their explanation. This is also true of 'tonic fits'. Quite possibly they may arise in the same centres as decerebrate rigidity (though Jackson did not assert this), but while simple rigidity may be regarded as 'release phenomenon', a tonic fit has all the appearances of an active and explosive discharge of energy, as an irritative phenomenon, in other words. These have always been carefully distinguished from simple release phenomena. That Wilson fails to draw this distinction is seen from his reference to Graham Brown's stimulation experiments on the red nucleus, as well as from his view that tonic fits are merely attacks of decerebrate rigidity.

In short, Wilson appears to include phenomena which have little or nothing in common, under the term decerebrate rigidity; he makes no reference to the most commonly seen forms of this condition; while the conditions of disease underlying the tonic states and involuntary movements comprehended within his definition include irritative lesions, diffuse and focal paralytic lesions, and, finally, hysteria.

At the same time, the rigidity and the tonic fits described are interesting and obscure phenomena, the elucidation of which is a problem of great physiological importance, and it is a distinct advantage that they should be considered as possible expressions of the tonic rigidity so fully described by Sherrington. This, however, has certain characteristics of incidence and quality, notably its plasticity and the reflex reactions that accompany it, and we should need a more minute description of these features in clinical cases than Wilson provides, before the identification could be attempted with any degree of accuracy. F. M. R. W.

**Roger, H.** Réveil hivernal de l'épidémie encéphalitique et revivescence saisonnière des encéphalites à forme prolongée. [**The winter incidence of epidemic encephalitis and the seasonal recurrence of chronic forms.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1921, **36**, 1633.

Roger draws attention to the almost exclusive incidence of lethargic encephalitis during the period November–March, in every country in which it has appeared, and for every year since 1916.

In addition, he records several personally observed cases, in which the onset of the disease during the winter 1919–20 was followed by the persistence of such symptoms as muscular (myoclonic) twitching, or the paralysis agitans syndrome. With the arrival of December 1920 these cases have shown a marked aggravation of their symptoms and the appearance of fresh manifestations of the disease.

One of these cases, as briefly recorded by Roger, provides an interesting case for commentary. During the winter 1918–19, the patient, a man, had a short illness ushered in by two days' fever and consisting of asthenia and diplopia lasting for two weeks. Recovery ensued, and the patient appears to have been in normal health until two months ago, when transient diplopia was noted. More recently a sudden apoplectiform attack ushered in an illness consisting in right hemiparesis, ocular palsies (not specified), and lethargy.

Doubtless, the diagnosis of encephalitis is justified in this case, but from the brief account given one is tempted to ask why not disseminated sclerosis or cerebral syphilis? F. M. R. W.

## PATHOLOGY AND BACTERIOLOGY

**Twort, F. W. Researches on dysentery.** *Brit. J. Exper. Path.*, 1920, **1**, 237.

Three types of special forms can be isolated from dysentery and allied bacilli. Type A shows moderately thick but long bacilli, which may twist like a spirochaete. Type B shows long thick rods, some swollen in the middle or at one end, and these may break open and set free granules. The bacilli are associated with round forms and many free granules. Type C bacilli are like Type B, but shorter. There are many granules and round forms, also thick branching units. In older cultures most of the units are globular, and the protoplasm may collect as a semi-lunar mass round the circumference. A filter-passing dissolving material may be present in cultures of dysentery bacilli, &c., which breaks down the bacilli into granules. The special types A, B, and C are produced by normal bacilli, but some smaller units are always present. The special forms are probably not stages in a true life-cycle, as the normal type is not produced in rotation, and it is doubtful if they are mutations. Special types may be produced for performing special work, and types in 'pure culture' may be likened to bees in a swarm. They are possibly of importance in connexion with incubation period, successful infection, and production of immunity. Sexual multiplication is not proved, but may exist in normal cultures. P. F.

**Tocunaga, H.** Ueber die Biologie der Influenzabazillen. [**The biology of the influenza bacillus.**] *Deutsche med. Wchnschr.*, 1920, **46**, 1357.

An investigation into the effect of haemoglobin upon the growth of *B. influenzae*. Pfeiffer and all workers up to now have looked upon the iron-containing pigment fraction of haemoglobin as the essential body for growth, but the present author concludes that it is not this pigment but the globin fraction which is necessary. He arrives at this by showing that the haematin fraction will not allow growth, a fact which has been known always, while globin prepared by him from haemoglobin permitted good growth. Although the method of preparation ascribed would not be expected to produce pigment-free globin (Reviewer), nevertheless his specimens 'on analysis showed no iron reaction'. Method not stated.
P. F.

**Mackie, T. J.**, and **Rowland, C. C. The value of simultaneous testing for the Wassermann reaction with two different antigens and the 'ice-box method'.** *Brit. J. Exper. Path.*, 1920, **1**, 219.

(1) The sensitiveness of the Wassermann reaction as here described can be increased, especially in early primary and treated cases, by testing simultaneously with a liver lecithin plus cholesterol antigen and a heart extract plus cholesterol antigen, i. e. a proportion of weakly positive reactions can be detected in this way which would escape notice if only one of these antigens were used. (2) The ice-box modification as applied to the method described does not confer any appreciable advantage over the usual procedure of incubating the mixture of antigen, serum, and complement at 37° C. for 1½ hours. P. F.

**Frühwald, R.** Ueber Spirochätenbefunde in Lymphdrüsen. [**Spirochaetes in lymphatic glands.**] *Wien. klin. Wchnschr.*, 1920, **33**, 999.

An estimate of the value of examining for spirochaetes in fluid removed by puncture of the regional glands, in the diagnosis of syphilis. This procedure is recommended in cases of primary syphilis in which the chancre is healing or has been treated with antiseptics. The syringe needle is pushed into various parts of the gland and a few drops of saline are injected. Aspiration is then started while the gland is being massaged.

In 24 cases of primary syphilis, *S. pallidum* was found in the inguinal glands 20 times, 7 times in 18 cases of acute secondary syphilis, and 7 times in 27 of later secondary syphilis.

Thus, in the hands of the author, the method is of very considerable value for the diagnosis of primary syphilis.

Attempts were then made to disclose spirochaetes in 'rests' in the glands of later cases of syphilis. Four tertiary glands were examined, but none were found.

Spirochaetes were, however, found in enlarged glands of two cases described as 'latent' (i.e. persons with no obviously conspicuous signs of syphilis at the moment, but not closely examined.—Reviewer). One had a positive W.R. and had syphilis 2½ years before; the other was a recent case of secondary syphilis, in whom the obvious signs had receded after a dose of salvarsan. P. F.

**Habermann, R.**, u. **Mauelshagen, F.** Die Bedeutung der Hoffmannschen Drüsenpunktion für die Früherkennung der Syphilis. [**The value of gland puncture in the early diagnosis of syphilis.**] *Deutsche med. Wchnschr.*, 1920, **46**, 574.

Thirty-three cases of primary syphilis were examined by gland puncture and in 30 *S. pallidum* was found. In 11 of the cases the method permitted an early diagnosis, which, otherwise, was impossible.

In the secondary period spirochaetes were not found so often. P. F.

**Dreyfus, G. L.** Die Beschaffenheit des Liquor cerebrospinalis—das entscheidende Moment für Prognose und Therapie in den einzelnen Stadien der Syphilis des Nervensystems. [**The constitution of the cerebrospinal fluid—the deciding factor for prognosis and therapy in syphilis of the nervous system.**] *München. med. Wchnschr.*, 1920, **67**, 1369.

A summary of the author's long-continued investigations into the relation of the state of the cerebrospinal fluid to the prognosis and treatment of cerebrospinal syphilis.

A pathological cerebrospinal fluid in the early stages of syphilis may revert to the normal without treatment; from the latent stages onwards, however, such a fluid is an index of grave progressive processes in the C.N.S. This is particularly so when the W.R. is positive in high dilutions. The author has observed in many cases a progression from cerebrospinal (interstitial) to generalized encephalitis (G.P.I.).

Eighty per cent. of 72 cases of early syphilis without obvious nervous signs show pathological cerebrospinal fluids (including slight increase of pressure as such). Most of these become normal on treatment, but some become abnormal again, and therefore it is essential in every case of syphilis to repeat lumbar puncture about 12 months after the end of treatment. The first course of treatment is vastly more important than subsequent courses for preventing relapse.

Among 260 'latent' syphilitics, without nervous signs, at all periods of infection 17 per cent. had abnormal cerebrospinal fluids.

Cases of cerebrospinal syphilis (371 cases) require intensive treatment in proportion to the degree of abnormality. Many cases can thus be brought to normal, but others not.

In tabes (327 cases) a normal cerebrospinal fluid may be found, but this does not necessarily indicate a cure of the process, and treatment should nevertheless be carried out.

The short summary of the author's work indicates again that no case of syphilis can be properly controlled or treated without the information supplied by repeated lumbar puncture. P. F.

**Bruusgaard, E.** Neurosyphilis. [**Neurosyphilis.**] *Norsk Mag. f. Lægevidensk.*, 1920, **81**, 76–84.

Professor Bruusgaard's main theses may be classified thus. (1) It is certain that an inadequate, unsystematic course of salvarsan treatment may be harmful, as it often gives an atypical turn to the disease, notably neuro-recurrence. (2) In the case of primary syphilis with a positive Wassermann, specific treatment must be pushed vigorously, and prolonged observation is required before the success of abortive treatment can be claimed. (3) In cases of primary syphilis with a negative Wassermann, modern specific treatment can almost invariably abort the disease and effect a complete cure. (4) If early cases of neuro-recurrence are traceable to inadequate specific treatment, then energetic, systematic treatment should banish this complication.

In support of hypotheses (1) and (4), B. gives the following statistics from the dermatological department of the Rigshospital in Christiania. Since 1912, 630 cases of recent secondary syphilis were observed, and among them were 10 cases of neuro-recurrence. After giving details of each of these cases, B. remarks that common to all was the inadequacy of the specific treatment. In some cases only a few injections of salvarsan or neo-salvarsan had been given at long intervals. In others numerous injections had been given, but the each injection had been small. At this point B. digresses with the reminiscence that his predecessor, Caesar Boeck, objected to the use of mercury in early syphilis because its course was only modified, and not always to the benefit of the patient. As for B.'s fourth hypothesis, he finds it supported by the fact that since he adopted, in 1915, energetic, systematic treatment of early syphilis, he has only once seen a case of neuro-recurrence among 420 cases of early secondary syphilis. His treatment for men and women was different. The former were given salvarsan combined with injections of salicylate of mercury, the latter neo-salvarsan combined with mercurial inunctions. The first course of treatment was the most energetic on the assumption that it might also be the last. Treatment was continued long after the disappearance of clinical symptoms and the development of a negative Wassermann. The total amount of salvarsan given in one course was often 5 to 6 grm., and of mercury up to 2 grm. For women the total was 6 to 10 grm. of neo-salvarsan, and often as much as 250 to 300 grm. of mercurial ointment. B. pushes the mercurial treatment of women more than that of men because the action of neo-salvarsan is far less effective than that of salvarsan. Referring to the one case of neuro-recurrence in this series, B. confesses that, had he but taken the precaution of examining the cerebrospinal fluid before the patient's discharge, this disaster might have been avoided. C. L.

**Holland.** Neurosyphilis. [**Neurosyphilis.**] *Norsk Mag. f. Lægevidensk.*, 1920, **81**, 84–7.

Discussing the prognostic significance of changes in the cerebrospinal fluid in syphilis, Holland regards globulin and an increased number of cells as of doubtful significance, for these two factors have not been adequately checked by control examinations in other diseases and in healthy persons. He attaches more importance to Wassermann's reaction. Lumbar puncture in 92 cases of recent syphilis was undertaken, the material, after the exclusion of 6 cases of congenital syphilis, being grouped in two classes. The first included 44 consecutive cases before the institution of treatment. In one case all three tests (globulin, cells, Wassermann) were positive, the patient being a man of 45, with headache as the only clinical symptom. In three other cases, one of the tests was positive, and in one case two of the tests (globulin and cells) were positive. The second series of cases included 42 patients on whom lumbar puncture was performed because clinical evidence, such as headache, suggested morbid changes in the cerebrospinal fluid. While only 5 of the patients in the first group showed morbid changes, 17, or 42 per cent., showed morbid changes in the second group. Holland gives these findings with reserve, admitting that they may prove instructive only in conjunction with similar investigations by other workers. C. L.

**Schou, H. J.** Nervelidelser ved tidlig Syfilis og deres Behandling. [**Nerve lesions in early syphilis and their treatment.**] *Hosp.-Tid.*, 1920, **63**, 57–9.

In a preliminary report to the Danish Dermatological Society, Schou reviews his findings in about 800 cases of syphilis of less than 3 years' standing. About 1,200 examinations of the cerebrospinal fluid was made, the number of cells, the amount of the proteins, and Wassermann's reaction being investigated. The cases were classified according as they had been treated or not, and according to the stages of the disease. There were 491 cases of recent syphilis in which absolutely no treatment had been given. Among them were 56 cases of primary syphilis with a positive Wassermann (blood), and in 12 per cent. morbid changes were found in the cerebrospinal fluid. The same percentage was found in 75 cases of primary syphilis in which Wassermann's reaction (blood) was negative. This percentage rose to 23 in 300 cases of secondary syphilis, and to 39 in 41 cases of syphilis of 6 to 12 months' standing. The cerebrospinal fluid showed morbid changes in 27 per cent. of the 15 cases of 1 to 2 years' standing. Schou notes as remarkable that most of the changes observed in the cerebrospinal fluid coincided with the second half-year of the disease. The changes found in the cerebrospinal fluid were, in the order of their frequency, pleocytosis, globulinosis (25 per cent.), a positive Wassermann (21 per cent.), and albuminosis (14 per cent.).

Altogether, 133 patients with primary and secondary syphilis were examined by a neurologist who found partial or complete loss of the abdominal reflexes in 9 per cent., exaggeration of the patellar reflexes in 20 per cent., and sensory disturbances of the trunk and lower limbs (of a uniform, radicular type) in from 5 to 10 per cent. Among patients with the triad: absence of patellar reflexes, lively tendon reflexes, and slight sensory disturbances, the cerebrospinal fluid showed morbid changes in 60 to 90 per cent., i. e. they were 3 to 4 times as common as in syphilitics not showing this triad. There would, therefore, seem to be some connexion between spinal meningitis and nerve symptoms. In about one-third of the cases of primary and secondary syphilis headache was present and was almost invariably associated with an increased intraspinal pressure. Optic neuritis was found in 3 per cent. of 443 cases of recent syphilis, and disturbances of the auditory mechanism in about 14 per cent. of 135 cases. Curiously enough, the cerebrospinal fluid seldom showed morbid changes in these cases—a fact suggesting that there is no connexion between lesions of the eye and ear and spinal meningitis.

To investigate the course of early syphilitic meningitis, Schou repeated lumbar puncture at intervals of a half to two months and found that, in 53 patients in the second stage, cerebrospinal fluid which originally showed morbid changes invariably showed diminution of these changes or their complete disappearance after treatment. But when it was normal to begin with, it subsequently showed morbid changes in a certain number of cases in spite of, or possibly because of, treatment. In 9 cases of primary disease examined again after an interval of a half to two months, the second lumbar puncture showed that a negative finding on the first occasion is very often followed by a positive finding on the second, although in the interval specific treatment has been vigorously pushed. In other words, certain changes in the cerebrospinal fluid tend, like Wassermann's reaction in the blood, to develop in spite of treatment. At one time the effect of this tendency was labelled 'neuro-recurrence', but it really is the expression of the further development of a slight attack of syphilitic meningitis. In 39 cases, 3 're-punctures' were made about a year after infection, and they showed that, whether the cerebrospinal fluid be 'positive' or 'negative' in the secondary stage, it will as a rule be 'negative' after a year. But, in a few cases, it will still be markedly 'positive', although, as a rule, the patient notices no effects thereof. Four 're-punctures' in 20 cases in which the disease had lasted 2 to 5 years showed the same phenomenon; in a certain proportion of cases latent syphilitic meningitis persists.

Discussing the proposition that these cases, in which the cerebrospinal fluid is abnormal, subsequently terminate in general paralysis and other nervous diseases of syphilitic origin, Schou remarks that this can hardly happen to all, for on clinical evidence only 10 to 15 per cent. of all cases of syphilis develop these late syphilitic lesions. The cases he suspects as being most liable to develop general paralysis, &c., are those in which the cerebrospinal fluid shows morbid changes directly after infection. There were 12 such cases among 500, i. e. 2·5 per cent. A second class of case which would probably be peculiarly liable to general paralysis, &c., would include those in which morbid changes in the cerebrospinal fluid persisted or relapsed. There were 6 such cases out of 60, i. e. 10 per cent. Adding this percentage to the 2·5 per cent. already referred to, he gets a ratio of 12·5 per cent. This, he points out, tallies with the ratio suggested by clinical evidence. He admits, however, that this selection of candidates for general paralysis, &c., is based on purely hypothetical grounds, and only systematic neurological examinations of many syphilitics conducted over a considerable period can control his hypotheses. C. L.

**Bordet, J.**, et **Ciuca, M.** Exsudats leucocytaires et autolyse microbienne transmissible. [**Leucocytic exudates and a transmissible bacterial autolysin.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1293.

**Bordet, J.**, et **Ciuca, M.** Le bactériophage de d'Herelle, sa production et son interprétation. [**The production and interpretation of d'Herelle's bacteriophage.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1296.

How are variations carried on to descendants to reproduce the characters of species? There must be a factor, induced by some external influence, which acts directly on a cell to cause a variation. When this factor is produced by the cell itself and operates continuously, it is easy to understand how a variation is established, so long as the causative external influence continues. When, however, this external influence only operates for a short time and then ceases after having excited the intracellular factor, we must assume that this factor is capable of regular rejuvenation from generation to generation in order not to lose its original energy. If the factor of variation could not propagate itself the variation would cease. In practice it must be presumed that the factor, in order to carry on its effect upon the cell, must be renewable by the variation it induces.

Suppose, now, that the cell is a microbe and that the intracellular factor inducing variation is an active substance produced by the microbe as a result of the fleeting stimulus of an external influence. We must deduce that the microbe must transmit the aptitude to form this substance to its descendants. If we further imagine that this substance is diffusible in a culture medium, the mere contact of a medium in which such a microbe has grown will confer the same variation upon allied microbes placed in the medium, and these in their turn to others, and so on *ad infinitum*. If the variation relates to the life or death of the microbe, it will be seen that the species may propagate indefinitely an aptitude, for instance, for autolysis.

If a guinea-pig is inoculated intraperitoneally with several doses of *B. coli*, the peritoneal fluid, when added to a normal culture of the same species, will confer upon it the power of autolysis, which is transmissible from culture to culture. The microbe in such a clarified culture may be killed by heat, but still the power of transmission of autolysis remains. The technique is as follows: the exudate from the guinea-pig is placed in a tube of broth and the few surviving microbes grow therein. The culture is now heated to 58° C. for 30 minutes and then diluted with several volumes of broth, reinoculated with *B. coli* and incubated for 24 hours at 37° C. and 2 or 3 days at room temperature. The culture tends to become clearer rather than more opaque. If this is now sterilized by heat, it is found either to prevent growth of *B. coli* or to lyse it if it has already occurred. Thus the species has developed the hereditary power of autolysis.

When a culture has been lysed a few bacteria still remain alive and when subcultured on to broth these grow very feebly, but when on to agar they may be trained to grow well. Such an agar culture has altered characters and does not lose its transmissible lytic power. It is more pathogenic for the guinea-pig than the original strain and is less readily phagocytosed. Further, 1 c.c. of an autolysed and sterilized culture injected into the peritoneal cavity of a guinea-pig will protect it from a dose of *B. coli* which kills a control in 8 hours.

In the second paper the authors point out that these phenomena explain the lytic action described by d'Herelle (and previously by Twort.—Reviewer) and ascribed by him to a living filter-passing virus which preyed on the microbes in a culture (vide *Medical Science*, 1920, **2**, 182). P. F.

**Thomsen, O.**, and **Wulff, F.** **Experimental studies of the mode of action of antimeningococcal serum.** *Acta med. Scandinavica*, 1920, **54**, 65.

The sera used by the authors were monovalent, prepared by injecting horses and rabbits with meningococci derived from Danish cases. 94 per cent. of these cases were of one serological type and differed from any of those described by Gordon in this country. The serum had a marked protective effect for mice and guinea-pigs if injected with or before the bacteria.

In order to arrive at an estimate of the therapeutic value of a sample of serum, it is necessary to know which immune factor is responsible for cure. Kraus and recently, in this country, Gordon have favoured the endotoxic factor, but the authors do not agree that an endotoxin is in question. They hold that meningococci do not multiply within the bodies of laboratory animals and that death occurs according to the volume of injected cocci as a consequence of poisoning by bacterial proteins.

When living meningococci are injected into the peritoneum of mice or guinea-pigs, they rapidly pass from the cavity into the blood-stream, and after 3 or 4 hours none are left. When the injection is intravenous the number in the blood-stream is rapidly reduced and they are found in the spleen, liver, and bone-marrow undergoing phagocytosis or autolysis, which latter leads to the poisoning of the animal. If, on the other hand, meningococci are injected into the peritoneum with serum, very few pass into the blood and these only just after injection. The animal is not poisoned. Similarly after intravenous injection the blood is found to be sterile after a few minutes.

To account for these phenomena, the authors were unable to find evidence of bacteriolysis. The reduced number of colonies on plating was due to agglutination and not to death of the cocci. Actually a marked agglutination occurs in the peritoneum, and this prevents the absorption of the cocci into the blood. After a short time these agglutinated cocci are phagocytosed, or immediately if leucocytes have been brought artificially into the cavity by a previous injection of aleuronate. This process does not actively kill the cocci, but they probably die out within the leucocytes by autolysis. The intracellular site of this autolysis accounts for the immunity of the animals against poisoning. After intravenous injection the same agglutination and phagocytosis occurs within the blood-stream, especially in the capillaries where the cocci are impacted.

The protective action of the serum is thus due both to agglutination and opsonization, the agglutinated cocci being more easily caught than if they remained as single units. The subsequent autolysis of the cocci, taking place within the leucocytes, does not lead to an intoxication of the animal. The endotoxic extracts of Kraus owe their toxicity to débris of meningococci, and the protective action of serum is due to an agglutination and phagocytosis of the débris. P. F.

**WALLGREN, ARVID. Acute leukaemia in pregnancy; an argument against the theory of infectious origin of the disease.** *Acta med. Scandinavica,* 1920, **54**, 133.

A very interesting and well-reported case of the rare combination of acute leukaemia complicated with pregnancy. The patient, aged 29, developed on October 28, 1919, a pain in the gums and observed a discoloured patch on the mucous membrane. The patch increased and she felt weak, and by November 6 was admitted to the Surgical Clinic in Upsala with the diagnosis of noma. A large lesion was found involving the gums and tongue, but there was no enlargement of glands or spleen. A blood examination showed 4,070,000 red corpuscles, 70 per cent. of haemoglobin, 10,800 leucocytes, of which 62·4 per cent. were of the large mononuclear (lymphoblastic) type. The neutrophils had sunk to 1·2 per cent. A few myelocytes were also seen. From the sudden onset, the gangrenous stomatitis, the fever, and the blood-picture the diagnosis of acute leukaemia was made. Of great interest is the fact that a year and a half previously she had suffered from haematemesis and several blood counts had been made, the last of which, on March 26, 1918, i. e. 19 months prior to the present illness, showed only an anaemia. She had been quite well until October 28, 1919. Daily examinations of her blood were made and showed a progressive deterioration from the count given above (November 6) until November 20, when the figures were 900,000 reds, 30 per cent. haemoglobin, 48,000 leucocytes, of which lymphoblasts numbered 87·8 per cent., lymphocytes 11·2 per cent., neutrophils 1 per cent., eosinophils 0·2 per cent., and myelocytes 0·2 per cent. On November 10 the patient, being in the 8th month of pregnancy, was delivered of a female child, and although there was some temporary improvement in her condition she died 11 days later. At the necropsy the changes in the viscera were slight, there was no enlargement of lymphatic glands. The marrow was of a pale brownish-red gelatinous appearance, and was mainly composed of large round non-granular cells of a lymphoblastic type. The normal structure of the lymphatic glands was obscured owing to the extensive infiltration of lymphoblasts among which some eosinophilic myelocytes were also found. The hepatic capillaries contained many lymphoblasts which were also found infiltrating the capsule of Glisson. The normal structure of the spleen was obliterated by the lymphoblastic and myelocytic infiltration. The necrotic part of the tongue was not infiltrated.

A searching examination of the tissues and organs of the child led the author to the conclusion that they were *normal*, at any rate not leukaemic. The author was able to find only three similar cases in the literature, viz. those of Askanazy (1893), Petersen (1914), Lindbom (1919), and he regards this as pointing to a non-infective origin of acute leukaemia. Reference is also made to the possible occurrence of acute leukaemia in newly-born children as reported by Pollmann (1897) and Lomell (1905). In both these cases the mothers were not affected with the disease. Obrastzow (1890) has recorded a case of acute leukaemia in a nurse who, shortly before, had attended a patient who died of the disease. W. B.

**McIntosh, J. Transmission of experimental encephalitis lethargica in series in monkeys and rabbits, with notes on a spontaneous infection in a monkey.** *Brit. J. Exper. Path.*, 1920, **1**, 257.

The successful transmission in series of experimental encephalitis lethargica to monkeys and rabbits has completed the experimental proof necessary to show that the disease is caused by a living virus. The spontaneous case recorded above is additional proof. In the second passage the inflammatory lesion was not quite so strictly localized. This is apparently due either to some change in the virus or to the lesion not being so advanced. The greater involvement of the cord is in keeping with the more diffuse nature of the brain lesion. P. F.

**Gramén, K.** Om Wildbolz' egenurin-reaktion för konstaterande av aktiv tuberkulos. [**Wildbolz's auto-urine test for active tuberculosis.**] *Hygeia*, 1920, **82**, 673–781.

Gramén has carried out Wildbolz's auto-urine reaction on about 40 cases of surgical and about 10 cases of pulmonary tuberculosis at the St. Göran's Hospital in Stockholm. Some healthy persons were used as 'controls'. In about 20 cases of definitely active tuberculosis, the reaction was positive, irrespective of the site of the tuberculous lesion. Among the cases in which surgical tuberculosis was more or less latent, the reaction was negative in about 50 per cent., and doubtful or faintly positive in the remainder. In some cases in which the disease was apparently healed, and also in some of the healthy 'controls', the reaction was positive; but Gramén discounts this evidence against the reliability of the test, pointing out that absence of clinical symptoms in apparently healthy persons does not exclude activity of a small focus of tuberculosis. His verdict on the whole is confirmatory of Wildbolz's findings. C. L.

**Maitland, H. B., Cowan, Mary L.**, and **Detweiler, H. K. The aetiology of epidemic influenza: experiments in search of a filter-passing virus.** *Brit. J. Exper. Path.*, 1920, **1**, 263.

During an outbreak of epidemic influenza at Toronto in the spring of 1920, 17 typical cases and 10 healthy controls were investigated to obtain evidence regarding a filter-passing organism as the cause of the disease. Whole blood, filtered plasma, filtered laked corpuscles, whole and filtered sputum and nasal washings, filtered empyema fluid, and filtered tracheal mucous membrane were used for animal inoculation. Guinea-pigs were principally used, but rabbits and mice also. Mice were found unsuitable. After inoculation the guinea-pigs and rabbits did not become ill, but showed, when killed, a constant type of haemorrhagic lesion in the lungs which has been described by Bradford, Bashford and Wilson, and Gibson, Bowman, and Connor, and construed by them as indicating experimental influenza in animals. There was also present a proliferative endothelial change as mentioned by the former group of authors. It was not always apparent to the naked eye, and was evidently of different origin from the haemorrhage, although sometimes associated with it. By reinoculation with filtered blood and lungs from such abnormal guinea-pigs, these lesions were repeated up to seven reinoculations. The same lesions and the same percentage of affected animals were found after inoculation with filtered blood from healthy persons. They were also present in apparently healthy guinea-pigs from their stock and breeding pens and in pigs that came to them from other laboratories, none of which had been inoculated. Attempts to obtain cultures of a filter-passing organism by special methods were unsuccessful. The animal lesions reported have no relation to the aetiological agent of epidemic influenza in man. Their aetiology is uncertain and is being investigated. P. F.

**Wolf, C. G. L. The influence of the reaction of media and of the presence of buffer salts on the metabolism of bacteria.** *Brit. J. Exper. Path.*, 1920, **1**, 288.

The effect of moderate concentrations of disodium hydrogen phosphate (2 per cent.) on the growth of *B. coli*, *Vibrion septique*, *B. welchii*, *B. sporo-*

*genes*, and *B. histolyticus* in glucose peptone has been investigated. The effect of acid potassium phthalate and sodium pyrophosphate on the growth of *B. coli* was also ascertained.

In all cases the buffer salt either partially inhibits gas production or produces a lag. If the fermentation be very prolonged, the volume of gas may finally approach that obtained from a non-buffered medium. The effect of phosphates on gas production is most pronounced in the case of actively saccharolytic organisms, but is also definite with proteolytic bacteria such as *B. sporogenes* and *B. histolyticus*.

The effect of phosphates on the nitrogen metabolism is not pronounced. On the whole the formation of amino-acids and ammonia from a medium containing peptones, polypeptides, and amino-acids is not increased.

In the case of the saccharolytic organisms the acid production appears to be increased when buffer salts are added to the medium. This bears out some of the results which have been obtained with similar organisms when fermentation takes place in the presence of calcium carbonate.

The final reaction of the fermentations is affected by the presence of buffer salts in the sense that in no case did the medium become so acid in the presence of buffer salts as it did when these salts were absent.

The toxin formation in *Vibrion septique* cultures is influenced by the presence of a buffer salt—sodium phosphate. The toxin had a higher potency than the control made without the salt. It is shown that toxins may be kept potent for long periods of time in the presence of sodium phosphate under conditions which would quickly destroy the toxicity of a product made in an unbuffered medium. **16** P. F.

**Collip, J. B. The effect of surgical anaesthesia on the reaction of the blood.** *Brit. J. Exper. Path.*, 1920, **1**, 282.

(1) The rate of elimination of water, acid and basic phosphates, and ammonia by the kidney, in periods before, during, and after anaesthesia, has been determined in a number of cases. (2) The acidity of the urine as estimated by this method is not materially altered during surgical anaesthesia. (3) A decrease in the $C_H$ of the blood during surgical anaesthesia is not indicated. (4) The acidity of the urine may be decreased during anaesthesia by the induction of hyperpnoea. (5) It is suggested that during surgical anaesthesia two processes, which are mutually antagonistic, are active, one the 'acidotic process' of Haggard and Henderson, due directly to disturbance in metabolism as a result of anaesthesia, the other the 'over-ventilation process'. Whether the $C_H$ of the blood falls, rises, or remains unchanged during surgical anaesthesia would therefore depend upon the relative intensities of these two processes. ($C_H$ is the hydrogen-ion concentration). P. F.

**Turnbull, H. M. Glycogenic infiltration of the liver of laboratory rabbits.** *Brit. J. Exper. Path.*, 1920, **1**, 310.

The histological changes seen in ordinary microscopic preparations of the rabbit's liver when infiltrated with glycogen after a suitable meal resemble closely those of a severe parenchymatous degeneration. The danger of mistaking in animal experiment these physiological changes for manifestations of degeneration is illustrated by an account of the findings in a series of experiments in which pairs of rabbits were inoculated respectively with contaminated water and with salvarsan dissolved in contaminated water. Incidentally, attention is drawn to the promising field offered by glycogenic infiltration of the liver of the rabbit for the experimental study of changes in the nucleus during physiological activity of the hepatic cell.

P. F.

**MENTEN, M. L. Variations in the benzidin peroxidase reaction depending on fixative, physiological activity, and type of animal.** *Brit. J. Exper. Path.*, 1920, **1**, 225.

(1) The Graham benzidin peroxidase reagent, consisting of a 0·5 per cent. solution of benzidin in 75 per cent. alcohol plus 0·2 per cent. hydrogen peroxide, produces a yellow-brown colour in the granules of myelogenous cells in human blood, and is diagnostic for man. (2) The polymorphonuclear leucocytes of blood of lower animals studied differ from those of human blood in their reaction to the Graham reagent in that only a small percentage of them develop the characteristic yellow colour. These positively reacting cells are probably eosinophilic. (3) In a 0·5 per cent. solution of benzidin in 75 per cent. alcohol free from hydrogen peroxide practically all of the myelogenous cells of the guinea-pig, dog, white mouse, white rat, and rabbit give the characteristic coloured granular reaction. Addition of hydrogen peroxide to this solution tends to inhibit the development of the yellow colour, which disappears from all except one or two cells when the concentration of the peroxide is increased to 1 per cent. (4) By varying the concentrations of the alcohols in the Graham reagent a series of colours ranging from deep brown through the yellows and the yellow-greens to blue may be obtained in granules of human pus aspirated from empyemic cavities. As these samples of pus age the colour reactions are lost. Pus in which the leucocytes become more degenerated give a negative reaction. (5) The blue reaction of pus-cells may be duplicated by exposing blood-films to weak concentrations of acid, previous to treatment with benzidin solutions.

P. F.

**RUSSELL, B. R. G., and WOGLOM, W. H. The respiratory exchange of surviving mouse tissues, normal and neoplastic.** *Brit. J. Exper. Path.*, 1920, **1**, 244.

Respiratory quotients were obtained for surviving normal and tumour tissues of the mouse by suspending emulsions in alveolar air in the Barcroft blood-gas apparatus. The results agreed very closely in successive experiments with each normal tissue. Greater variability was found with tumours.

| Normal. | | | Tumour. | |
|---|---|---|---|---|
| Kidney | 0·883 ± 0·002 | Rate of growth↑ ↓Differentiation | 37 S | 0·941 ± 0·010 |
| Liver | 0·813 ± 0·024 | | 206 | 0·868 ± 0·039 |
| Mamma | 0·914 ± 0·027 | | 63 | 0·818 ± 0·014 |
| Submaxillary gland | 0·841 ± 0·024 | | 113 | 0·951 ± 0·018 |
| (Total embryo | 1·3 – 1·1) | | 72 | 0·719 ± 0·031 |
| (Mouse embryo skin | 1·0) | | 155 | 0·674 ± 0·013 |

The tentative conclusion is drawn that the more rapidly growing, undifferentiated tumours draw their energy from carbohydrate, the more slowly-growing from fats.

P. F.

**Dragstedt, L. R. The effect of *Streptococcus hemolyticus* infection on the reaction of the blood of rabbits.** *J. Infect. Dis.*, 1920, **27**, 452.

This investigation was carried out to determine whether there is a change in the reaction of the blood during streptococcus infection, and whether, if there is a change, it is of sufficient magnitude to play any part in the course of the infection. Blood was collected from the marginal vein of the ear of a series of 30 normal rabbits. It was oxalated, dialysed through collodium sacs and the hydrogen-ion concentration of the dialysate was determined by the method of Levy, Rowntree, and Marriott. The range was found to be between $P_H$ 7·6 and $P_H$ 7·75. Strains of *Streptococcus haemolyticus* were injected into a series of rabbits intraperitoneally, and daily observations were taken of the general conditions, temperature, weight, and reaction of the blood. The maximum acidity observed during life was $P_H$ 7·3. When it is recalled that *S. haemolyticus* can grow in a medium with serum until the acidity reaches $P_H$ 4·63, the author concludes that the development of acidosis *per se* in an acute infection can play no inhibitory part in the progress of the infection. W. B.

**Meader, P. D., and Robinson, G. H. Biological and physical properties of the haemotoxin of streptococci.** *J. Exper. M.*, 1920, **32**, 639.

The production of haemolysin (haemotoxin) by certain streptococci has been the subject of a great deal of experimental study. The present authors, working with streptococci obtained from cases of empyema, have investigated particularly the effect of filtration, adsorption, centrifugalization, and shaking on the haemotoxin. Likewise they studied the influence of the composition and the reaction of media on the production of haemotoxin. They consider that it is a labile substance affected detrimentally by filtration or by shaking. It is adsorbed by both organic and inorganic compounds. It is obtained from bouillon having a $P_H$ value, at the time of testing, of 7·2 to 5·3. The authors consider that it exists free in the culture medium and that for its production two substances, at least, are necessary. One is phosphorus, while the other was not determined with precision. The unknown substance was present in considerable quantity in blood-serum and infusion of kidney, but it was neither albumin nor globulin metaprotein, primary or secondary protease nor peptone of the medium. The substance was found to be removed to a considerable extent by filtration through kieselguhr. W. B.

**Gay, F. P., and Morrison, L. F. Experimental streptococcus empyema. II. Attempts at dye therapy.** *J. Infect. Dis.*, 1921, **28**, 1.

In a previous communication (vide *Medical Science*, 1920, **2**, 357) one of the present authors, Gay, in association with Stone, described the experimental production, in rabbits, of empyema from the injection of *Streptococcus pyogenes* and the production of an active immunity from the use of vaccines. Continuing this line of work the present paper of Gay and Morrison deals with the bactericidal action of dyes on streptococcus, and especially the therapeutic value of dyes which exhibit powerful bactericidal properties *in vitro*. Thirty different dye-stuffs were tested for bactericidal powers on streptococci in broth culture as well as in pus. Eight of these in dilutions of 1 : 20,000 or more killed the cocci in both fluids. The bactericidal titre was greater in broth than in pus with two exceptions.

Acriflavin killed streptococci in pus in a dilution of 1 : 200,000, while in broth the titre was 1 : 20,000; proflavin destroyed the cocci in both fluids at a dilution of 1 : 200,000. Experimental empyema in rabbits was produced by injecting 0·2 c.c. of a 24-hour-old broth culture of a passage strain of *Streptococcus pyogenes* into the right pleural cavity. Between passages the culture was kept in the ice-box. The therapeutic experiments consisted in the injection of the dye into the pleural cavity on the day following the introduction of the culture. The dyes employed were saffranin, janus green, solid green, methylene blue, new fast green 3 B, and acriflavin. In spite of the fact that the doses injected were larger than appeared to be theoretically necessary to sterilize the pus, and although there was no evidence of decomposition of the dye-stuff, the life of no animal thus treated was prolonged. W. B.

**Richards, J. H. Bacteriologic studies in chronic arthritis and chorea. Part I. Arthritis.** *J. Bact.*, 1920, **5**, 511.

This is a very abridged account of 'part of a study of chronic arthritis undertaken to determine whether any constant cultural or immunologic streptococcus was associated with this disease'. The investigator defines, by exclusion, the type of joint affection dealt with, but by his own definition the joints included constitute not one but many types of disease as this is understood clinically. In all, 104 patients were examined. Blood cultures were made in all these and *Streptococcus viridans* was identified in 14. No other bacterium was found, and the controls examined gave negative results. The information with regard to this part of the investigation is more complete than that given regarding any subsequent part. Controls are not mentioned subsequently in the account of the investigation, and even here it is not stated how many controls were employed.

Complement fixation tests were also done in the whole series. The antigen used was the unkilled, thoroughly washed, salt-ground, bacterial emulsion, the dilution being determined by estimating their nitrogenous content. Positive results were obtained in 68.

Cultures were taken from the fluid from joints in 54 individuals, this being done during an acute exacerbation, and an attempt was made to obtain fluid also from the periarticular tissues. Of these 54, *Streptococcus viridans* was isolated in 4, but no information is given of the presence or absence of other organisms.

The faeces were examined by the Gram stain in all the cases. Streptococci were found in 42 and of these *Streptococcus viridans* was identified in 4.

The gums of all the members of the series under observation were examined bacteriologically, the pus being obtained from a pyorrhoea or from the socket of a freshly drawn tooth, and *S. viridans* was found to be present in 50. Again no mention is made of healthy controls.

The tonsils, whose secretion was cultivated in all of the 104 cases, gave a positive result for *S. viridans* in 40. Certain sinuses, the prostate, the pelvis of the kidney, and the Fallopian tubes accounted for 9 positive cultures of this streptococcus. Presumably the foci mentioned in the last group were examined only in those individuals where the clinical evidence pointed to the possibility of infection, but no definite information is available on this point. The question is nevertheless an important one, as, not infrequently, joint troubles co-exist with an accidentally discovered focus of infection in one or other of these situations.

The results, on analysis, are of themselves sufficiently remarkable, for of 104 patients examined only 9 showed an entire absence of association with *Streptococcus viridans*. They are still more remarkable when we consider the relative infrequency and lack of pathogenicity of this particular micro-organism. They are, however, arresting, if we may infer that the investigator's cases were taken indiscriminately in accordance with his own classification, because this would not include only the so-called infective type of chronic arthritis, that group to which some would confine the term 'rheumatoid arthritis', occurring before middle life and showing many affinities with other diseases of known bacterial origin. It would embrace also not only types which, clinically at least, show very little evidence of being infective, but even certain joint diseases which are almost certainly non-bacterial. It is true that, in his introductory classification, the author divides chronic arthritis into those cases which are 'non-bacterial in origin' and those which are 'associated with bacteria in origin'. This, however, is a mere begging of the question, for there is no definite proof that any belong to the latter group with the almost sole exception of tubercular and the gonococcal joints.

Further, if one judges by the recorded ages of the patients selected for the purpose of this investigation, very few are included which belong to the class already mentioned whose clinical resemblances to bacterial diseases are relatively pronounced.

The report, however, is obviously a highly condensed one. Without an accurate clinical description of each individual examined, in the existing chaotic state of chronic joint classification, such records are not of very much assistance either to the clinician or to other investigators.

R. S. W.

**Avery, O. T., and Cullen, G. E. Studies on the enzymes of pneumococcus. I. Proteolytic enzymes. II. Lipolytic enzymes: esterase. III. Carbohydrate-splitting enzymes: invertase, amylase, and inulase.** *J. Exper. M.*, 1920, **32**, 547, 571, 583.

The first paper is concerned with the study of the proteolytic enzymes of pneumococcus. These enzymes are intracellular, and are capable of hydrolysing (to some extent) intact protein, and especially peptones, the latter with striking avidity. Sterilization as a rule was performed by autoclaving for 20 minutes at 15 lb. pressure. $P_H$ values were determined colorimetrically, with the series of indicators outlined by Clark and Lubs. Total nitrogen determinations were made by Kjeldahl's method, while amino-nitrogen was determined by van Slyke's nitrous acid method. Peptide nitrogen, viz. that in the —CO.NH— linkings was determined by splitting them into amino-acids by hydrolysis and then finding the increase in amino-nitrogen.

The optimum reaction for hydrolysis is $P_H$ 7 to 7·8, which also represents the optimum for the growth of pneumococcus. The terms 'protease' and 'peptonase' are used, but with no assumption as to whether proteolysis and peptolysis are due to two separate enzymes or are two activities of the same enzyme. Solutions of intracellular substance of comparable enzymic activity may be prepared by dissolving the bacteria in bile, in sodium choleate, or by mechanical and autolytic disintegration of the cell. The rapidity with which peptone is hydrolysed is proportional to the concentration of the enzyme. The enzyme is sensitive to heat; an exposure for 10 minutes at 100° C. destroys its activity. If the acidity is increased to $P_H$ 5, the acid death-point of pneumococcus, it suspends activity, but does not destroy the enzyme, for the activity is restored by a readjustment to $P_H$ 7·8. Attenuation of virulence to one-millionth of its original strength had no measurable quantitative effect on the enzyme activity.

In the second paper evidence is put forward to show that pneumococci possess also an endolipase of marked activity. The substrate used to demonstrate the lipolytic action was tributyrin. In no instances were antiseptics used as preservatives in the digestion mixtures, while sterility of all enzyme-substrate solutions was proved by subculture. The ordinary method of adjusting the substrate to approximate neutrality with phenolphthalein, and then to determine by titration the amount of acid produced by the enzyme action, was not adopted. The authors found the optimum hydrogen-ion concentration for lipolysis, and then maintained this reaction by suitable buffer solutions. This buffered substrate maintains optimum conditions for enzyme action with a minimum of inhibition due to the acid products of hydrolysis. The enzyme-containing solutions were obtained by dissolving pneumococci in bile, or by extraction by other means. The optimum reaction above mentioned was about $P_H$ 7·8, agreeing again with the optimum for the growth of pneumococcus. If the enzyme is heated for 10 minutes at 70° C. its activity is destroyed. Attenuation of the virulence of the pneumococcus had no measurable effect on enzyme activity. Enzyme solutions preserved at refrigerator temperature retain their activity for weeks. The possible relation of the endolipase to the mechanism of bile solubility is discussed.

In the third paper the authors investigate the action of the intracellular carbohydrate-splitting enzymes, amylase, invertase, and inulase. The avidity with which pneumococcus attacks certain carbohydrates is manifest in the accelerated growth and increased acid production of organisms cultivated in the presence of these substances. Acids are produced in culture media from starches and glucosides, as well as from mono- and di-saccharides. The simple expedient of dissolving the bacterial cells in bile and testing the resultant solution for the presence of enzymes as carried out above for proteolytic and lipolytic activity was here found unsatisfactory. This was due to the fact that bile in the concentration necessary to effect bacterial solution inhibits completely the activity of the enzymes which convert sugar and starch. As a result, the authors disintegrated the pneumococcal cells by suspending them in balanced phosphate solution of $P_H$ 6·2, and hastening physical disruption by repeated freezing and thawing of the bacterial suspension. It was found that the enzymes present could act on sucrose, starch, and inulin. Determinations of $CO_2$ content were made by van Slyke's apparatus. Qualitative tests for reducing sugar were carried out with Benedict's solution, while qualitative determinations were made by Benedict, by rotatory power, or by the gravimetric copper method. The iodine colour test was used for the hydrolysis of starch to dextrins. Sterility controls were used in all cases. The invertase and amylase of pneumococcus are active within the limits $P_H$ 5 to 8, with an optimum at $P_H$ 7·0. This range corresponds closely with limiting hydrogen-ion concentrations which define growth of the organism in the presence of carbohydrate. Attempts to determine the presence of an enzyme or enzymes capable of fermenting dextrose and producing acid, an active characteristic of the growing cell, were unsuccessful. The authors conclude that the enzymes described are not true secretory products of the living cell, but are of the nature of endo-enzymes, since their activity can only be demonstrated when cell-disintegration has occurred. W. A. M. S.

**Thomsen, O.**, and **Christensen, S.** Bidrag til kendskabet af pneumococtyper. [**A contribution to the study of the types of pneumococci.**] *Hosp.-Tid.*, 1920, **63**, 729-39.

Thomsen and Christensen have found by agglutination tests that the types of pneumococci described by Americans as Types I, II, and III, are identical with types occurring in Denmark. The marked differences between these types were demonstrated on mice; a highly virulent culture of pneumococci was thought to belong to Type I only, as it was agglutinated by I serum but not by II or III serum. It was, therefore, anticipated that 0·1 to 0·2 c.c. of I serum would protect against 0·05 to 0·1 c.c. of a 24-hour-old, highly virulent bouillon culture. But the mice invariably died, and the blood, spleen, and peritoneal exudate teemed with pneumococci.

It was found that all the colonies obtained from this source belonged to Type III. Thus, the culture, supposed to contain only Type I, had evidently become infected with Type III pneumococci: but these had formed such a small proportion of the pneumococci in the culture that they showed no *visible* agglutination by III serum. When a strictly pure culture was obtained by Burri's method of culture from a single pneumococcus, then 0·2 c.c. of the corresponding serum protected mice against 0·05 to 0·1 c.c. of a 24-hour-old bouillon culture.

To ascertain whether Type III was absolutely unaffected by I serum, solutions of 24-hour-old bouillon cultures of pure I and III types were made up to 0·5 c.c. by the addition of 0·2 c.c. of I serum plus physiological saline solution. Table I shows the effects of intraperitoneal injections of varying quantities of Types I and III cultures into 16 mice. It was found that 0·2 c.c. of I serum protected against 0·05 c.c. of Type I culture, whereas such a minute dose as 0·0000001 c.c. of Type III caused fatal infection, acting in the same way as on mice given no serum. The conclusion drawn from these experiments was that the various types of pneumococci are as different from each other serologically as the other micro-organisms to be found in the sputum. Hence the necessity for type-specific serum in the treatment of pneumococcal infections.

In order to learn how small a proportion of one type in a mixed culture of Types I and III would be demonstrable by agglutination, solutions containing the types in different proportions were made from equally dense bouillon cultures of Types I and III, and were tested with I and III serum. It was found that, when one type formed only 20 per cent. of the mixture, it was incapable of agglutination, and this was not demonstrable till the type in minority represented at least 40 per cent. of the mixture. When the two types were present in equal quantities, agglutination was equally well-marked with I and III serum. There was a tendency, demonstrated in different ways, for Type I to outgrow Type III during passage from one mouse to another by intraperitoneal injection. This difference in the behaviour of the two types was shown by the following experiments.

Six mice were given intravenous injections of various quantities of Type III. Six other mice were given intraperitoneal injections of the same quantities. It was found that the intravenous injections were considerably less toxic than the intraperitoneal injections. But when this experiment was repeated with Type I, there was no difference in the effect of intravenous and intraperitoneal injections. This difference in the behaviour of Types I and III was not demonstrable when highly virulent were replaced by only slightly virulent cultures. Probably the greater resistance of the mouse under certain circumstances to intravenous, as compared with intraperitoneal, injections may be traceable to the blood containing more bactericidal or growth-inhibiting substances than the peritoneal fluid.

Using Burri's method for isolating single pneumococci, Thomsen and Christensen introduced into the peritoneal cavity of two mice 3 and 5 pneumococci respectively, belonging to Type I. Both mice died, after 2 days, of pneumococcal septicaemia, with Type I in the blood. The same experiment with 5 and 4 pneumococci of Type III caused no infection. More than 4 or 5 couples of pneumococci could not be counted with accuracy, but it was found that at least about 20 pneumococci, counted by Wright's method, of Type III were required to provoke infection by peritoneal injection. These experiments, again, suggest that a greater degree of virulence can be achieved for Type I than for Type III. Type I differed markedly from Types II and III in the slightness of the precipitation by its homologous serum of a bouillon culture freed from bacteria by centrifugalization. The precipitation of bouillon cultures of Types II and III by II and III sera respectively was marked, that for Type II being slightly greater than that for Type III.

C. L.

**Dumas, J.** Sur la présence du bactériophage dans l'intestin sain, dans la terre et dans l'eau. [**On the presence of bacteriophage in the healthy intestine in soil and in water.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1314.

**d'Herelle, F.** (1). Sur le microbe bactériophage. [**On the bacteriophagic microbe.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1318.

**d'Herelle, F.** (2). Sur la nature du principe bactériophage. [**On the nature of the bacteriophagic principle.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1320.

**Bablet, J.** Sur le principe bactériophage de d'Herelle. [**On the bacteriophagic principle of d'Herelle.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1322.

**Debré, R.**, et **Haguenau.** Quelques particularités du 'phénomène de d'Herelle'. [**Some peculiarities of the 'd'Herelle phenomenon'.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1348, 1368.

**Wollman, E.** (1). A propos de la note de MM. Bordet et Ciuca. (Phénomène de d'Herelle, autolyse microbienne transmissible de J. Bordet et M. Ciuca et hypothèse de la pangenèse de Darwin.) [**Concerning the note of Bordet and Ciuca. (d'Herelle's phenomenon, transmissible microbic autolysis of Bordet and Ciuca and Darwin's theory of pangenesis.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1478.

**Wollman, E.** (2). Sur le phénomène de d'Herelle. [**On the phenomenon of d'Herelle.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 3.

**Salimbeni.** Sur le bactériophage de d'Herelle. [**On d'Herelle's bacteriophage.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1545.

The fundamental observations on which is based d'Herelle's idea of the existence of a 'bacteriophagic' microbe which produces a lysis of *B. dysenteriae* Shiga have already been reviewed in this journal (*Medical*

*Science*, 1920, **2**, 182). In the same review attention was directed to the work of Kabeshima, who disputed d'Herelle's main contention that the 'bacteriophage' was living, as he found that it sustained without injury a temperature of 70° C. Kabeshima considered that it was probably of the nature of a catalyst which caused micro-organisms to produce autolytic ferments, these ferments acting as catalysts to other bacteria. In this way the lytic or bacteriophagic process can be carried on from generation to generation. Twort, who was in fact the first to recognize the bacteriophagic phenomenon (1915), had a similar idea. Upon all new subjects in science, a literature, good and bad, rapidly accumulates, and this is now happening with regard to the 'phenomenon of d'Herelle'. It is taking one of two directions, (*a*) new facts illustrating bacteriophagic phenomena, (*b*) new views explaining these phenomena. Some of the recent communications are here considered.

Dumas describes the bacteriophagy of *B. dysenteriae* Shiga and *B. coli*, from products obtained from persons who never had intestinal disease. He also found 'bacteriophage' in the intestine of guinea-pigs, and, believing it to be widely disseminated, examined and found it in soil and in different waters. Thus, on adding 150 c.c. of water to 150 c.c. of bouillon and placing the mixture in the incubator for 24 hours, he found that the filtrate from a Chamberland bougie is lytic when tested on *B. dysenteriae* or *B. coli*.

d'Herelle (1), in a short note, defends his previous position in opposition to Kabeshima, and maintains that the alleged solubility of 'bacteriophage' in ether is not a reality. In a second note he considers in particular the idea of Kabeshima that the action consists essentially of a catalyst and a proferment, the latter being present in or produced by the bacterium, while the former is derived from the host. d'Herelle thinks that the transmission from generation to generation must be due to a living agent endowed with powers of reproduction.

Debré and Haguenau examined 81 samples of faeces from 63 persons, and, having prepared the bacteriophagic materials by filtration, as usual, tested them on dysentery, paratyphoid, typhoid, and colon bacilli. In 6 cases of acute dysentery the intestinal filtrate was active three times. In 16 cases of enteric fever it was also found three times. It was also present in material from one case of diarrhoea, one of cancer of the stomach, one of rheumatic fever, one of phthisis, and two cases of peritonitis. On the other hand, Debré and Haguenau found no evidence of bacteriophage in filtrates from the stools of infants healthy or ill, breast- or bottle-fed. They also affirm that the bacteriophagic extracts are not always of the same activity in different persons or even in one and the same person at different times. Seventeen 'strains' of bacteriophage studied by them were all active on *B. dysenteriae* Shiga. While the bacteriophage acts in a medium, such as bouillon or serum, it is inactive if applied to an emulsion of Shiga's bacilli suspended merely in salt solution.

An important communication of Bordet and Ciuca on this subject has been separately reviewed in this number of *Medical Science*. In a short note Wollman recalls the resemblance between Bordet's views and the old doctrine of pangenesis by Darwin. Salimbeni points out that facts, similar to those established by d'Herelle, are known in connexion with myxomycetes and myxobacteria, which only live in association with certain bacteria and, having grown, cause lysis of the said bacterium. He cites the case of *Dictyostelium mucoroides*, which lives in association with *B. fluorescens.*

From cultures of *D. mucoroides*, Pinoy obtained a ferment which was lytic for *B. fluorescens*. Salimbeni thinks that the d'Herelle phenomenon is really due to some stage in the history of a pleomorphic organism. He carried out observations on the lysis of *B. dysenteriae* Shiga by 'bacteriophage', examining the changes induced in a van Tieghem chamber. He found, in addition to the dysentery bacilli, a number of small, round or slightly elongated bodies. The latter were often seen in direct contact with the bacilli. They germinate and set at liberty small masses of protoplasm which for a time remain attached to the bacilli. Having ultimately freed themselves, the protoplasmic masses enlarge and show one, rarely two, vacuoles, and throw out pseudopodia and, as he affirms, become myxamoebae. These changes can also be studied in stained preparations. Salimbeni provisionally suggests the name of *Myxomyces shigaphagus* for his myxamoeba. In a note A. Pettit states that Dumas, whose research is referred to above, on examining his cultures in the light of Salimbeni's report, found that a number of the tubes contained a myxamoeba.

In a later communication, Wollman (2) has made some interesting experiments to determine the nature of d'Herelle's phenomenon. If one add a trace of a living culture of Shiga's bacillus to a diluted bacteriolysate it is observed that there is a great increase in the bacteriolytic power, and this power is preserved for a long time, even in the absence of living Shiga bacilli. Wollman then studies what the effect would be if the bacilli were separated by a membrane which would be permeable to a ferment-like body but impermeable to bacteria like *B. dysenteriae.* Such a membrane may be made in the form of collodium sacs. These are prepared in the ordinary way and are connected with a small glass tube plugged with cotton wool, the sacs having been sterilized in water in the autoclave at 110° C. The water which has diffused into their interior having been removed by a pipette, is replaced by bouillon inseminated with a trace of *B. dysenteriae*, and the charged sac is lowered into a tube of bouillon to which has been added 10 drops of an active bacteriolysate. If one adds a drop of this bouillon-diluted bacteriolysate to a living culture of Shiga's bacillus and implants the mixture on agar, at once or later, areas of lysis make their appearance. With very permeable collodium sacs charged with *B. dysenteriae* in the interior, lysis takes the place of the bacilli, from which, it is contended, there must have been a passage of the bacteriophagic element through the collodium. In the interior of the sacs Salimbeni is stated to have found elements such as he had previously reported.

With less permeable sacs (4 per cent. collodium) employed in the same manner as above, it was found that the bacteriophage in the bouillon, i. e. outside the sac, increases in activity, but there is no lysis of *B. dysenteriae* in the inside of the sac, a result which is interpreted as being due to the fact that the bacteriophage has multiplied outside the sac but has not penetrated into the interior. Wollman considers that this experiment renders untenable the view that the process is a modification of the bacillus as suggested by Bordet and Ciuca. W. B.

**NINNI, C.** Ricerche sulla flora del tenue intestino di piccoli erbivori, specialmente in rapporto alla presenza in esso del *B. coli.* [**On the flora of the small intestine of small herbivora, with special reference to the presence in it of *B. coli.***] *Pathologica*, 1920, **12**, 242.

Investigations were carried out on healthy and diseased guinea-pigs

and rabbits, and showed the following results: (1) the addition of 0·2 per cent. of glucose to 1 per cent. peptone water is sufficient to obtain a production of indol in 24-hour cultures of *B. coli.* (2) Such an addition allows one to ascertain the presence of *B. coli* in many instances (stomach of healthy guinea-pigs and rabbits) in which it would have not been identified by means of the ordinary methods. (3) *Bacillus coli*, which cannot be identified by any means in the duodenum of healthy guinea-pigs and rabbits, is always found in great quantities if the animals are even slightly diseased.
C. d. F.

**Davison, W. Divisions of the so-called Flexner group of dysentery bacilli.** *J. Exper. M.*, 1920, **32**, 651.

The author briefly records the results he obtained in the examination of a large number of strains of dysentery bacilli of the Flexner type. He tried to group the strains by agglutination and fermentation tests, and while agreeing with the recent English workers that there are divisions of the Flexner group, he considers that they are ill-defined and do not appear to be sufficiently distinct to warrant the use of separate names. He thinks that all mannitol-fermenting dysentery bacilli should be called *B. dysenteriae* Flexner and the subdivision noted. The subdivision should be either by carbohydrate fermentation or by agglutination with monovalent rabbit serum, but not by both, as they do not coincide.
W. B.

**Di Macco, G.** Sulla efficacia del nutrosio nel terreno nutritivo di Drigalski-Conradi. [**On the influence of nutrose in the culture medium of Drigalski-Conradi.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 71.

The author has studied comparatively the growth of *B. typhosus*, *B. paratyphosus* A and B, *B. coli communis*, and *B. dysenteriae* (Shiga and Flexner strains) in the Drigalski-Conradi culture medium prepared with and without nutrose. From many painstaking measurements it resulted that only the colonies, both superficial and large, of *B. typhosus*, cultivated in Drigalski's agar with nutrose, are somewhat larger than those seen in the same medium but without nutrose. All other bacteria investigated grew into colonies of the same size. Hence the general conclusion that the addition of nutrose to the Drigalski-Conradi medium is not necessary for the growth and identification of the bacterial species mentioned above.
C. d. F.

**Fred, E. B., and Peterson, W. H. The fermentation of xylose by bacteria of the aerogenes, paratyphoid B and typhoid groups.** *J. Infect. Dis.*, 1920, **27**, 539.

Teague and Morishima, among others, have shown that the pentose xylose is fermented by *B. typhosus* without gas formation, by *B. paratyphosus* B with gas, and is not attacked by *B. paratyphosus* A. The present authors have made a study of the actual substances formed, including in their series of bacteria *B. aerogenes*, which also produces gas. With this latter organism carbon dioxide and ethylic alcohol were found to represent about 75 per cent. of the sugar consumed. The main products of the fermentation of xylose by *B. paratyphosus* B are formic, acetic, butyric, lactic, and succinic acids, ethyl alcohol, carbon dioxide, and hydrogen, these products representing about 92 per cent. of the original sugar. The fermentation of xylose by *B. typhosus* is far from complete, not more than one-fourth of the sugar being attacked. Only small quantities of carbon dioxide are formed. The greater part of the fermented xylose is represented by succinic acid, although alcohol, formic, acetic, and butyric acids are among the other products. The medium employed in these researches consisted of a fresh yeast water extract containing 0·5 per cent. dibasic potassium phosphate and 0·5 per cent. Difco peptone. The amount of xylose added was 2 per cent. W. B.

**Ornstein, M.** Zur Bakteriologie des Schmitzbazillus. [**On the bacteriology of the bacillus of Schmitz.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **91**, 152.

During the war K. E. F. Schmitz described an organism closely resembling *B. dysenteriae* Shiga, but differing from it in its ability to form indol and in the fact that it is not agglutinated by Shiga serum. Schmitz's bacillus also gained notoriety through the statement of its discoverer that pure cultures underwent remarkable transformations in that they became converted into *B. typhosus*, *B. paratyphosus* B, *B. dysenteriae* Shiga, *B. coli*, *B. coli mutabile*, *B. faecalis alkaligenes*, and even other bacteria. The present author, Ornstein, has made an elaborate study of Schmitz's bacillus based on the examination of 31 strains, 8 of which were isolated in the Hygienic Institute in Frankfurt, where the work was carried out, while 23 strains were obtained from Schmitz. The author considers that Schmitz's bacillus is a well-characterized species, and in his hands none of the conversions into typhoid or other bacteria, as described by Schmitz, occurred. In the course of the investigation two bacteria were encountered which were liable to be mistaken for the bacillus of Schmitz. The first of these is named by the author *Bacillus fallax*, a name which has no standing, seeing that it was already used by Weinberg and Séguin, 1915, for a thoroughly characteristic, obligate, spore-bearing anaerobe. Ornstein's *B. fallax* differs from Schmitz's bacillus in being able ultimately to ferment saccharose. It also turns litmus whey of a deeper blue colour and is antigenically distinct. The second newly-described micro-organism it is proposed to call *Bacillus inconstans* on account of its variable behaviour in the presence of dextrose. Occasionally it acts on this sugar with gas formation. At other times it is unable to do so. Antigenically it is also distinct. On saccharose-fuchsin-sulphite-agar plates *B. fallax* (Ornstein) and *B. inconstans* both show mutations like *B. coli mutabile*. According to the author, Schmitz's bacilli in the living state do not show acid agglutination although killed cultures are very variable. *B. fallax* and *B. inconstans* as a rule both show marked acid agglutination in living as well as in dead cultures. Difficulties were experienced in preparing high grade agglutinating sera against Schmitz's bacillus, although in the presence of such sera all the strains of the bacillus behaved alike. Anti-Schmitz serum possesses complement-fixing properties in combination with cultures of the homologous organism, but none in the presence of *B. fallax* or *B. inconstans*. The experiments which the author cites indicate that in all probability *B. inconstans* is not a well-defined species. The pathogenic properties of Schmitz's bacillus on animals were not striking. W. B.

**Dold, H.**, und **Fischer, W.** Ein Fall von natürlich erworbener, bazillärer Dysenterie beim Hunde mit gleichzeitiger Schistosomiasis, Ankylostomiasis und Filariosis. [**A case of naturally acquired bacillary dysentery in the dog with simultaneous schistosomiasis, ankylostomiasis, and filariasis.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, **85**, 198.

A report on the occurrence of bacillary dysentery in a young male German pointer in Shanghai. The animal was observed to be ill and to be passing mucus and blood in its liquid stools. An examination revealed the presence of vegetative amoebic forms, eggs of *Schistosomum japonicum* and *Ankylostomum*, while in its blood microfilariae were found. On the ground of finding amoebae, emetin was given subcutaneously, but the animal became rapidly worse and died in a few days. At the autopsy typical Shiga bacilli were found, the anatomical changes showing a diffuse acute pseudo-membranous inflammation over the whole intestine, large and small. The amount of actual ulceration was, however, comparatively slight. The intestine was also infected with *Schistosomum* and *Ankylostomum*, and *Dirofilaria immitis* was also found in the blood. Nephritis and hypertrophy of the heart completed the anatomical picture. *Entamoeba histolytica* was not found. The authors suggest that the animal was probably infected from human dysenteric faeces, as these dogs are extensively used for hunting game in the low-lying grossly contaminated ground of the Yang tse and the Hwang pu rivers. W. B.

**Eiskamp, E. H.**, and **Park, L. K.** **Fate of micro-organisms introduced into isolated loops of the intestine.** *J. Infect. Dis.*, 1921, **28**, 67.

In this research dogs were employed. The abdomen being opened, a ligature was placed round the duodenum immediately below the pylorus. The duodenum was then flushed out with warm salt solution introduced through a hypodermic needle inserted immediately below the ligature. The salt solution having been gently forced along by a milking movement, a 20 to 30 cm. loop of the empty duodenum was isolated between ligatures, the loop always including the bile and pancreatic openings. Jejunal loops were isolated in a similar manner. Emulsions of various bacteria were injected into the loops, and after gentle massage a control sample was removed and counted for bacteria. The abdomen was then closed, and after a period of 2 to 12 hours the animals were killed and the contents of the loops again examined to see what changes had taken place in the numbers of the bacteria which had been previously introduced. The results were based on the examination of 26 animals. Many of the bacterial cultures employed were of saprophytic type, but pathogenic organisms like *B. typhosus*, *S. aureus*, *Streptococcus*, and *B. anthracis* were also employed. It was found that many of the microbes introduced had been destroyed. By a study of the bacteria other than those experimentally introduced, the authors concluded that the destruction is not due to any antagonism of the bacteria normally found in the bowel. They think, indeed, that there is another and distinctive antibacterial mechanism, the nature of which, at present, is unknown. W. B.

**Beckwith, T. D.**, and **Lyon, R. H.** **The viability and growth of *B. typhosus* in bile.** *J. Infect. Dis.*, 1921, **28**, 62.

A very large literature exists on the effects of bile and bile salts on members of the colon-typhoid group of micro-organisms. The present authors have again dealt with the subject, and have endeavoured to find out whether *B. typhosus* is viable in bile and whether it can multiply freely in this medium. Seven samples of bile were tested, five being human, one from the rabbit, and one from the ox. Known quantities of typhoid culture were introduced into bile, and plate-cultures were made at successive intervals up to as long as 48 hours. The results showed that *B. typhosus* is long lived in human, rabbit, or ox bile. Introduced into sterile ox bile it is subjected at first to marked bactericidal activity on the part of the medium, by which a large number of bacilli are destroyed. This is followed by an evident lag, and finally there is a slow but progressive proliferation. W. B.

**Litch, V. M.**, and **Meyer, K. F. A spontaneous epidemic among laboratory rabbits caused by a paratyphoid B bacillus related to the rodent group.** *J. Infect. Dis.*, 1921, **28**, 27.

This is an account of a small epizootic, in laboratory rabbits, due to a paratyphoid organism belonging to the animal paratyphoid group. The details which are of interest to laboratory workers should be consulted in the original. It may be pointed out, however, that the micro-organism isolated did not belong to the human paratyphoid group from an antigenic point of view. The fact that it was able to produce a toxin may be of importance in connexion with outbreaks of food-poisoning in man from the consumption of rabbit. Hitherto the chief, if not the only, instance of this has been the occurrence of paratyphoid in four persons, including a child of 4 months, which was described by MacConkey in 1906 (*J. Hyg*, **6**, 570). By cultural and agglutinating experiments he showed that the microbe isolated from a piece of the suspected rabbit and from the spleen of the child, who had only partaken of a small quantity of the gravy, was closely related to *B. aertrycke* and *B. paratyphosus* B.
W. B.

**Behmer, W.** Beiträge zur Biologie und Biochemie des *Bacillus proteus* und Versuche zur Isolierung pathogener Mikroorganismen aus proteushaltigem Material mittels Agarplatten mit Karbolsäurezusatz bzw. Eichloffblauplatten. [**The biology and biochemistry of *B. proteus* and attempts at the isolation of pathogenic bacteria from *Proteus*-contaminated material by means of agar plates containing carbolic acid or Eichloff-blue.**] *Arch. f. Hyg.*, 1920, **89**, 295.

The author made an exhaustive examination of 23 strains of *Proteus*. The primary object of the work, however, was to elaborate a satisfactory technique whereby various bacteria could be isolated from mixtures containing *Proteus*. Hitherto the most satisfactory method has been that of Schaeffer, who found that 2 c.c. of a 5 per cent. solution of carbolic acid per 100 c.c. of agar afforded a medium on which *Proteus* grew as isolated well-defined colonies instead of spreading over the whole culture surface and making isolation of other bacteria almost impossible. Carbolic acid medium has, however, drawbacks, for certain bacteria will not thrive upon it. A substitute is described by the author under the name 'Eichloff-blue'. This term is meant to indicate that the medium is blue from litmus and is made of an extract of a proprietary article, from skimmed milk, manufactured by Eichloff in Greifswald. The medium is identical with that of Drigalski and Conradi except that, instead of meat extract, the extract of Eichloff is employed. On 'Eichloff-blue' plates *Proteus* colonies are smaller than on carbolic agar and are well defined, and it possesses advantages in that certain organisms which will not grow on carbolized media will grow well on the new medium suggested. *B. anthracis* will not grow on either medium. W. B.

**Amoss, H. L., Gates, F. L.,** and **Olitsky, P. K. Simplified production of antimeningococcic serum.** *J. Exper. M.*, 1920, **32**, 767.

This paper deals with attempts to produce a more efficacious antimeningococcic serum and considers the fundamental basis on which antimeningococcic sera have hitherto been prepared. It is now thoroughly well established that the general term meningococcus really covers a group of closely related micro-organisms and is not a fixed antigenic entity. So long ago as 1909 Dopter separated meningococci from parameningococci, and this differentiation was further extended to two other groups by Gordon, who separated four different types. The practical question from a therapeutic point of view is whether antimeningococcic serum should be made with one or many antigenic types. For example, the antimeningococcic serum of the Rockefeller Institute has been made as polyvalent as possible, cultures to the number of 51 having been employed in its manufacture. The present authors have now studied antimeningococcic sera made with a few or actually a single strain of meningococcus and have compared the agglutination reactions with those of the polyvalent serum of the Rockefeller Institute, in which a large number of strains have been utilized in the immunization. They found that horses injected with an antigen limited to five, three, or one strain of culture yielded sera with a range of agglutinins covering in high dilutions practically all the stock strains used in making the polyvalent serum.

Very striking differences were observed, for whereas the agglutinating power of the highly polyvalent serum remained unimpaired after storage for a year, a monovalent serum fell off greatly in this period, especially with regard to secondary or subsidiary agglutinins. A serum made with five strains, viz. a regular meningococcus, a parameningococcus, and three intermediate meningococci approached the Rockefeller polyvalent serum, and at the end of a year still agglutinated 39 of 41 strains tested. Absorption tests also brought out striking differences in the nature of the polyvalent and monovalent sera which had appeared to be identical in simple agglutination tests. The homologous strain on triple absorption was able to exhaust the monovalent serum completely, but was unable to remove from the polyvalent serum agglutinins to which 30 out of 44 different strains were able to react. In addition to specific agglutinins, a monovalent serum contains a wide range of common or secondary agglutinins, but these tend to disappear on keeping. The difference between specific and secondary agglutinins is only apparent in absorption tests. In a serum produced by the injection of a large number of strains the agglutinins are mostly specific and differ in some way from the secondary agglutinins which make their appearance in sera which have been produced with one or a few strains. The authors did not determine whether the two types of sera had different therapeutic powers. W. B.

**Anderson, John F. An improved method for the production of antimeningococcic and other serums.** *J. Infect. Dis.*, 1920, **27**, 482.

Hitherto the production of antibacterial sera has been associated with considerable difficulties, among which may be mentioned the prolonged period required and the loss of animals from toxic or other causes. The author has had a large practical experience, and discusses in particular the anaphylactoid phenomena witnessed in horses during immunization against meningococci for therapeutic purposes. He appears to have got over this difficulty by the use of antigens washed, free of poison, in salt solution, the injections, which are intravenous, being made immediately after the bacteria have been so treated. The severe and even fatal reactions after intravenous inoculation are apparently due to the presence of some toxic substance and are not really manifestations of a true anaphylactic character. The scheme of immunization suggested provides for four successive intravenous injections with intervals of three days, the treatment being commenced with dead bacteria which after the fourth injection is changed to living cultures. W. B.

**De Witt, Lydia M. Weight curves of tuberculous guinea-pigs.** *J. Infect. Dis.*, 1920, **27**, 503.

The authoress draws attention to the fact that in most of the experimental work on the chemotherapy of tuberculosis the apparently beneficial results of treatment are based on increased duration of life, favourable influence on weight and diminished distribution and progress of the disease in the animals employed. The present paper is an attempt to determine whether the weight curves of guinea-pigs inoculated with tuberculosis constitute a satisfactory basis for the expression of an opinion on the therapeutic value of any drug. The weights of normal guinea-pigs, tuberculous untreated and tuberculous treated guinea-pigs are given in tables and in curves. Normal guinea-pigs of approximately the same age and weight, and living under the same conditions run a uniform weight curve. This curve is, however, easily modified by changes in diet, acute infections, and other variations in the conditions of life. Normal male guinea-pigs of approximately the same age and weight, inoculated with the same doses of the same strain of T.B. and maintained under the same conditions subsequently run a fairly uniform and typical weight curve. This may therefore be employed in testing the effects of various methods of treatment and is a more sure guide than the duration of life. Most therapeutic remedies tested, even although so non-toxic that they did not exert an influence on the duration of life, or on the weight curves of normal guinea-pigs, tend to produce a material alteration in the type of the weight curve. This alteration consists in the main of a diminution in height of the ascending curve and an increase in length of the descending curve. W. B.

**Metalnikow, S.** L'immunité naturelle et acquise chez la chenille de *Galleria mellonella*. [**On natural and acquired immunity in the larva of *Galleria mellonella*.**] *Ann. de l'Inst. Pasteur*, 1920, **34**, 888.

For a number of years Metalnikow has made experiments on the effect of introducing diverse strains of tubercle bacilli into the larvae of *Galleria mellonella*—the bee moth. He described the existence of a powerful phagocytic mechanism by means of which the creature was enabled to deal with colossal doses, which were without effect. Some of the more recent work of Metalnikow and Fiessinger were reviewed in this journal (*Medical Science*, 1920, **2**, 575). There it was pointed out that Fiessinger had shown that although there was abundant evidence of intense phagocytosis in the larva, the tubercle bacilli were not necessarily killed, for after a sojourn of eight hours in the larva they were still pathogenic for the guinea-pig. The present communication of Metalnikow is virtually a *résumé* of his previous work with certain additions. He gives a full account of the phagocytosis and capsule formation whereby the tubercle bacilli become segregated and immobilized, and he points out that the brown masses formed in this process may persist from the larval to the imaginal state. With regard to the destructive powers of the phagocytes, he quotes experiments on three guinea-pigs inoculated with the contents of larvae which, five days previously, had been injected with a large quantity of living T.B. Only one of the guinea-pigs died of tubercle, and he thus infers that at least a portion of the introduced bacilli must have been killed. Among other observations in his interesting paper Metalnikow cites the fact that, although tetanus and diphtheria toxins are powerless to injure the larvae, snake venom or ox bile, even in minute quantities, are almost instantly fatal. Mammalian red corpuscles were harmless, even of heroic doses. In spite of multitudes of experiments Metalnikow has never found evidences of the formation of any antibodies in the larvae operated upon. Although *Proteus* cultures are extremely fatal to larvae, they are so only on injection into the interior of their bodies. Animals infected with or dead from *Proteus* are incapable of starting an epizootic when placed among the healthy. W. B.

**KONGSTED, ELIZABETH.** Vergleichende Untersuchungen über die Methoden von Herman und von Ziehl-Neelsen zur Färbung von Tuberkelbazillen. [**The comparative value of the methods of Herman and Ziehl-Neelsen for staining tubercle bacilli.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, Orig. **84,** 513.

In 1889 Martin Herman recommended for staining tubercle bacilli a mixture of crystal violet, alcohol, and ammonium carbonate. The violet and alcohol constituted one solution and before use was added to the solution of ammonium carbonate. Nitric acid and 95 per cent. alcohol were used as the decolorizing agents. In 1908 Herman modified his method and recommended a mixture of 1 part of a 3 per cent. solution of crystal violet in 95 per cent. ethylic alcohol and 3 parts of a 1 per cent. watery solution of ammonium carbonate. The strain was heated for 1 minute at boiling-point. Decolorization was brought about by 10 per cent. nitric acid, followed by 95 per cent. alcohol. As a counterstain, eosin (1 per cent.) was used. Many workers have used this method as it stands or with trivial modifications, and in general have found it gives a higher percentage of positive results than the Ziehl-Neelsen method. The present authoress has employed it, alongside the Ziehl-Neelsen method, in the examination of 1,200 specimens of sputum of which 345 were positive. Of these 29 were positive only by Herman's stain and 8 were positive only by the Ziehl-Neelsen method. The number of T.B. in 136 specimens were alike with both stains. In 125 cases there were most bacilli with Herman's and in 47 more with the Ziehl-Neelsen method. W. B.

**Lichtenstein, Stephanie.** Ein Fall von spontaner Froschtuberculose. [**A case of spontaneous tuberculosis in the frog.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, **85**, 249.

In the course of experiments on frogs the authoress found one with a nodule on the liver. Smears therefrom showed masses of acid-fast bacilli like T.B. Pure cultures were easily obtained, and were found to produce a miliary form of tuberculosis disseminated everywhere, although usually more sparse in the lungs. Death took place in 3–8 weeks. Cultures were also lethal in about 12 weeks to *Molge cristata*. There is a discussion on the literature of frog tuberculosis. W. B.

## BIOCHEMISTRY

**Drummond, J. C.,** and **Coward, K. H. Researches on the fat-soluble accessory factor (Vitamin A). VI. The effect of heat and oxygen on the nutritive value of butter.** *Bio-Chem. J.*, 1920, **14**, 734.

The authors corroborate the results reported in this number by Hopkins by showing that destruction of fat-soluble vitamine takes place through oxidation. C. G. L. W.

**Hopkins, F. G.** (1). **The effect of heat and aeration upon the fat-soluble vitamine.** *Bio-Chem. J.*, 1920, **14**, 725.

Fats are purified in various ways in order to make them edible, and some discussion has taken place as to the effect of heat on their vitamine content. The author shows that fat-soluble vitamine is quite resistant to heat, withstanding a temperature of 120° C. for four hours if protected from air. If exposed to a temperature of only 80° C., and air is bubbled through the fat at the same time, destruction of the vitamine proceeds with considerable rapidity. Even exposure of the fat in thin layers to the air at room temperature results in its losing its capacity for promoting growth. The vitamine is prone to oxidation by atmospheric oxygen.

C. G. L. W.

**Hopkins, F. G.** (2). **Note on the vitamine content of milk.** *Bio-Chem. J.*, 1920, **14**, 721.

In his original paper on growth factors, Hopkins showed the effects of adding quantities of milk so small that they could not possibly influence the total amount of food given, and therefore it was necessary to look for some unsuspected substance in this type of food. Mendel and Osborne found it difficult to repeat these results. On repeating his older results, Hopkins found that there are certain seasonal variations which permit the growth factor to be exercised at one time and not at another. Where the difference comes in has not been definitely ascertained. C. G. L. W.

**Stephenson, M. A note on the differentiation of the yellow plant pigments from the fat-soluble vitamine.** *Bio-Chem. J.*, 1920, **14**, 715.

A good deal of interest has been attached to the physiological significance of the yellow colouring matters found in certain plants such as carrots, which have been found to be identical with the yellow colours in body fat, corpus luteum, &c. It has been suggested that this substance was practically the same as the fat-soluble vitamine. In order to settle this question Miss Stephenson prepared the colouring matter in a fairly pure condition from a large quantity of carrots. This preparation proved effective in promoting growth in rats. When, however, pure carotene was prepared from the roots and fed in the same concentration as above, growth did not take place as in the first experiment, and the animals suffered from keratomalacia. The removal of the yellow pigment from butter fat did not interfere with its growth-promoting qualities. While carrots contain a growth factor, this substance is certainly not identical with carotene.

C. G. L. W.

**Zilva, S. S. The action of ozone on the fat-soluble factor in fats.** *Bio-Chem. J.*, 1920, **14**, 740.

Ozone inactivates the fat-soluble growth factor in fats. Ultra-violet rays did not impair the activity of the preparation. C. G. L. W.

**Drummond, J. C., Golding, J., Zilva, S. S.,** and **Coward, K. H. The nutritive value of lard.** *Bio-Chem. J.*, 1920, **14**, 742.

Lard has always been signalized for its lack of fat-soluble vitamine in contradistinction to other animal fats. The authors have endeavoured to determine the cause of the deficiency, for it might be due to the nature of the food used for fattening. or to the method of preparation for household use. Five groups of animals were placed on diets with various vitamine content. The final weights of the animals varied from 84 pounds on a deficient diet to 150 pounds with a full diet with grass. After killing, the fats from the slaughtered animals were incorporated in the diets of rats. The fats from the deficient animals were deficient in vitamine. Those which had received a full diet with grass contained a store of vitamine. The deficiency is therefore partly due to the method of fattening in this country. The second cause of loss is due to the method of manufacture of lard, which is exposed in the process to high temperature and oxygen.

C. G. L. W.

**Daniels, A. L.,** and **Loughlin, R. Deficiency of heat-treated milks.** *J. Biol. Chem.*, 1920, **44**, 381.

The authors found that milk, if raised quickly to the boiling-point, and kept there for one minute only, was quite adequate for growth. However, they could not get normal growth in rats upon milk pasteurized for 35–40 minutes, or treated in other ways which involved rather prolonged heating. As the vitamines (fat-soluble and water-soluble) seemed to be intact, they looked for other deficiencies, and came to the conclusion that the error in the milk, exposed to prolonged heat, was an inorganic one. The calcium salts were rendered more or less insoluble, so that the animals were being starved of calcium phosphates. The results are now being applied to infant nutrition. R. A. P.

**McCann, W. S. An observation of the effect of a protein meal given to a man at the end of an 8-day fast.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 173.

After a fast of 8 days a man was given a meal consisting of 350 grm. of meat and 10 grm. of butter. Very low respiratory quotients were obtained, viz. 0·687 and 0·681. These are what one finds in severe diabetes. The author explains these quotients by assuming that the carbohydrate portion of the protein is stored up in the depleted organism as glycogen. In diabetes the glucose is excreted; under the above circumstances it is stored up. C. G. L. W.

**Lusk, G. Additional experiments showing the production of fat from protein.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 171.

By direct and indirect calorimetric estimations it was shown that after a large meal of meat a dog retained carbon which could only be deposited in the form of fat. C. G. L. W.

**Bradley, H. C.,** and **Felsher, H. Studies of autolysis. VI. The effect of certain colloids upon autolysis.** *J. Biol. Chem.*, 1920, **44**, 553.

There is always interest attaching to the process of autolysis, by which a tissue undergoes spontaneous disintegration after death. There is a suggestive relation between autolysis and normal katabolism. The authors have found that the autolysis of such substances as beef-liver is in general markedly accelerated by acid. There are extant some observations by Ascoli and Izar to the effect that colloidal sols of metals, such as silver and gold, exercise a marked accelerating effect upon autolysis. These observations seemed to suggest an interesting relation between the colloidal state and enzyme action, and appear to be an exception to the rule of acceleration by acid. Unfortunately, upon repeating the work of Ascoli and Izar, the authors cannot obtain any of the effects which they have reported.

R. A. P.

**Tisdall, F. F. Estimation of the phenolic substances in urine.** *J. Biol. Chem.*, 1920, **44**, 409.

A good history of the research upon phenolic substances in urine is given in this paper. Using an ether extraction method for the estimation of the total phenolic substances in urine, results are obtained 50 per cent. lower than those recorded by Folin and Denis. The amount of volatile phenols (phenol and para-cresol) found by Tisdall's method agrees with the values obtained by Mooser and Hensel. It is suggested that the discrepancy between Tisdall's results and those of Folin and Denis is due to the presence in the urine of unidentified bodies which react with their reagents. The compounds are partly present in the free state and partly formed by the action of strong mineral acids on the urine. R. A. P.

**Wishart, M. B. Experiments on carbohydrate metabolism and diabetes. III. The permeability of blood corpuscles to sugar.** *J. Biol. Chem*, 1920, **44**, 563.

The author finds in dogs no specific alteration of the distribution of sugar between the blood-plasma and corpuscles in experiments with different quantities and modes of administration of glucose, different degrees of pancreatectomy and diabetes, lipaemia, acidosis, exercise, cold, or different renal thresholds. The concentration of sugar in the corpuscles is normally lower than that in the plasma, and holds for several animal species examined.

[It is curious that the author does not seem to be aware of a paper published by Falta and Richter-Quittner (*Medical Science*, 1920, **2**, 94), in which it was shown that, normally, corpuscles contained no sugar. Sugar passed into the corpuscles owing to a change of permeability produced in the collection of the blood sample, unless it was collected by treating with hirudin and centrifuging rapidly. No mention is made here of the method of collection.] R. A. P.

**Kipp, H. A. Variation in the cholesterol content of the serum in pneumonia.** *J. Biol. Chem.*, 1920, **44**, 215.

The substance cholesterol seems to have a mysterious relationship to many important body processes. For instance, diminutions in the cholesterol content of the nerves have been found to occur in acute inflammatory conditions; there are further obscure connexions between the antitoxin and antihaemolytic content of serum and the cholesterol content. The author gives a rather full history of work on cholesterol in these connexions. In this contribution he has studied the cholesterol content of serum in cases of pneumonia, using Bloor's methods. Though the figures show somewhat large variations, there seems, in pneumonia, to be a fall in the cholesterol content of the serum in the early stages of the disease. This is followed by a rise in cholesterol content during the period of convalescence, and for a short time after the period of resolution. Subsequently there is a return to the normal. It is considered by the author that the primary decrease in cholesterol is due to an absorption of the substance by the leucocytes and subsequent transport by them to the seat of inflammation. Here it acts as an antitoxic substance neutralizing toxins, and possibly exerting antigenic properties. In ordinary acute toxic infections, the utilization of cholesterol is proportional to the severity of the disease. The intervention of empyema in pneumonia disturbs the normal serum picture. R. A. P.

**Lewis, D. S.,** and **Mason, E. H. The diastatic ferments of the blood.** *J. Biol. Chem.*, 1920, **44**, 455.

Magendie (1846) showed that blood could split starch to dextrose and glucose. In 1867, Michael Foster reported a diminished excretion of diastatic ferment in diabetic cases, pointing out that the diastatic power of urine was not due to bacteria. Diastases are universally distributed in the body (pancreas, salivary gland, liver, blood, lymph, muscles, and kidneys). After complete removal of the pancreas the blood diastase quickly drops, returning, however, to its normal level in 4–5 days. This fact indicates that the pancreas is not the only supplier of diastase in the body. The interesting question is whether the blood diastase is connected with the hyperglycaemia of diabetes and nephritis or whether its presence in the blood is to a certain extent accidental. Research upon this point has been rather contradictory. Several observers have found no relation between disease and blood diastase, while others, such as Myers and Killian, have reported a series of diabetic cases showing a close relation between the level of blood diastase and the severity of the disease. The authors here find that the normal diastatic index is between 14 and 25, showing very little change in relation to food. In diabetes, they cannot find any constant increase in blood diastase. In cases of nephritis, though there are variations in the amounts of the ferments, there is no real relation between the severity of the lesion and the diastatic index. R. A. P.

**McLean, F. C., Murray, H. A., Jr.,** and **Henderson, L. J. The variable acidity of haemoglobin and the distribution of chlorides in the blood.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 180.

Completely deoxygenated blood was exposed to various tensions of carbon dioxide, first in an atmosphere with oxygen present and then in an atmosphere free from oxygen.

The whole blood was then analysed for oxygen and carbon dioxide free and combined, and the serum analysed for carbon dioxide and chlorides. The atmosphere to which the blood was exposed was analysed for carbon dioxide and oxygen. The conclusion reached from the experiments is that whenever the heterogeneous acid-base equilibrium is disturbed the new equilibrium is established by the migration of acids in and out of the cells, and about two-thirds of this acid is hydrochloric acid. The haemoglobin displays different degrees of acidity at varying oxygen tensions. The buffer action of the serum under physiological conditions as compared with isolated serum is increased at least ten times by the change in the acidity of haemoglobin. C. G. L. W.

**Horiuchi, Y. Studies on blood-fat. I. Variation of the blood-fat constituents of rabbits under normal conditions. II. Lipaemia in acute anaemia.** *J. Biol. Chem.*, 1920, **44**, 345.

Boggs and Morris showed how experimental lipaemia (increase of fat in the blood) could be produced in rabbits by drawing 15 to 45 c.c. of blood from them daily. This paper deals with the increase in the several fatty constituents (including lecithin and cholesterol) induced in rabbits by small daily bleedings and by one large bleeding. Rabbits fed on fatty and fat-free diets have been compared. Bleeding caused a very large increase in the fatty constituents of the blood; in one case, that of an acute anaemia produced by a single large haemorrhage of 45 c.c., the whole blood looked like chocolate cream. With regard to the duration of this type of lipaemia, a maximum is reached at the end of 72 hours after the bleeding. After this, the blood fat declines. The author considers that the increase is due either to food fat or tissue fat accumulating in the blood, support for this view coming from the more ready appearance of fat in the blood in the animal fed on a fatty diet. The increase in lipoids occurs in the plasma and not in the corpuscles in the case of rabbits, a slightly different result from that obtained by Bloor when working on certain human diseases. In explanation of the phenomenon, attention is drawn to a decrease of the amount of lipase in blood-serum found by Sakai. Haemorrhage may interfere both with the production of lipase by the pancreas and with the lipolytic activity of the liver and other organs. R. A. P.

**Imrie, C. G.,** and **Graham, S. G. Fat content of embryonic livers.** *J. Biol. Chem.*, 1920, **44**, 243.

The paper is a contribution to the question of the function of the liver in fat metabolism. It has been found that when fatty infiltration of the liver is produced by the injection of such substances as phlorrhidzin the accumulating fat tends to be comparatively highly saturated, resembling in iodine value the fat of the connective tissues. On the other hand the fat entering into the structure of the cell has a high iodine value. This is taken to mean that there is a mobilization of fat from the subcutaneous tissues in these cases.

Using young guinea-pigs, Imrie and Graham have shown that at a certain stage of embryonic development a fatty infiltration takes place in the embryonic livers without change in the fat content of the maternal liver, or difference in iodine value from the maternal liver fat. Consequently such fat cannot have been mobilized directly from the tissues. An explanation suggested is that the fat has been previously desaturated by the maternal liver or other tissues. The fat is used within 2 or 3 days after birth, and so is presumably a ready store. If tissue fat is mobilized in the pregnant animal by the injection of phlorrhidzin, an accumulation of fat of *low* iodine value (like tissue fat) accumulates in the embryonic liver. This may be independent of any similar change in the maternal liver. The experiments are suggestive, but do not really settle where desaturation of fat in these cases takes place. R. A. P.

**Lynch, V. Chemistry of the whitefish sperm.** *J. Biol. Chem.*, 1920, **44**, 319.

Of the chemistry of the head of the spermatozoon not much is known and is bound to be interesting ultimately from many points of view. The dried sperm heads of the whitefish were found by Lynch to contain about 70 per cent. nuclei and 30 per cent. protamine. All the phosphorus, 6 per cent., was combined with the nucleic acid. The protamines gave a xanthoproteic reaction, but did not give the test for tyrosin, cystin, or tryptophane. If true, it would suggest that these latter amino-acids are not essential to life.

R. A. P.

**Cullis, W. C.**, and **Hewer, E. E. The ‘ammonia coefficient’ of pregnancy.** *Bio-Chem. J.*, 1920, **14**, 757.

In a case of pregnancy terminating successfully without induced labour, the ratio of ammonia to total nitrogen rose to 77·9 per cent. This ratio is higher even than the well-known one of Nebelthau of 66 per cent. The total acid part of nitrogen at the time was very small (2·1 grm.).

There appeared to be no relationship between the vomiting and the coefficient. The results confirm earlier observations in the same field by Ewing and Wolf (*Amer. Journ. Obst.* 1907, **55**, 289). C. G. L. W.

**Wilson, D. W. Studies in pyrimidine metabolism.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 179.

When uracil nucleoside is administered to rabbits there is often more nitrogen excreted in the urine than can be accounted for by the nucleoside. The same happens with a mixture of cytosin and uracil nucleoside. Increasing quantities of uracil appear in the urine, or simpler complexes containing the uracil group are fed. The conclusion may be drawn that in the metabolism of yeast nucleic acids the pyrimidine group is early changed in such a way as to yield urea. C. G. L. W.

**Barbour, H. G., and Baretz, L. H. Temperature changes induced by gum acacia injections in normal and fevered animals.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 209.

The pyrexia induced by injection of pactopeptone and *B. coli*, and by puncture of the corpus striatum, was depressed by the injection of solutions of 7·0 per cent. gum acacia. The effect is fleeting. A small rise in temperature takes place in normal animals after its injection. C. G. L. W.

**Maltaner, F., and Hoppe, E. N. Osmosis as a factor in the local accumulation of leucocytes in the body.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 216.

Chemical forces have generally been held responsible for the chemotaxis of leucocytes. It is asserted by the authors that the forces which come into play are physical. Leucocytes were found to move in the direction of the osmotic force and opposite to the direction of the diffusing substances in solution. This motion is explained as being due to the greater permeability of leucocytes for water, and the fact that their total mass is negligible as compared to their content of water. C. G. L. W.

**Cheplin, H. A., and Rettger, L. F. Studies on intestinal implantation of *Bacillus acidophilus*.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 192.

*B. acidophilus* is found in the intestinal tract normally in very small numbers. If two grammes of lactose or dextrin be given to rats for two to six days, a complete transformation of the flora takes place which is strongly dominated by *B. acidophilus*. This also takes place with human subjects. The administration of 300 grm. of lactose or dextrin led to an almost complete suppression of all other viable bacterial types. The change may also be brought about by giving milk soured by the organism. A non-gas-producing flora is obtained thereby. The effect was much more pronounced than with *B. bulgaricus*. C. G. L. W.

**Gudernatsch, J. F., and Bagg, H. J. Disturbances in the development of mammalian embryos caused by radium emanation.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 183.

By the injection of 5 millicuries of radium emanation, contained in a small amount of saline solution, into pregnant and non-pregnant rats, no monstrosities were produced, but a definite effect was seen on foetal and placental tissue. The embryos are killed, and, instead of being aborted, remain attached to the uterine wall and are gradually absorbed. When the foetuses were removed peculiar haemorrhagic areas were noticeable along the dorsal mid-line. These extravasations take place in the vessels of the subcutaneous connective tissue and along the meningeal sinuses. Numerous haemorrhagic areas were found in the uteri and especially in the ovaries. Weak doses of radium emanation did not produce any macroscopically visible effects on the maternal tissues. The embryonic differentiating tissues were affected. This fact may be of some biological significance, for it is known that radium rays have a decided effect on fast-growing tumour and cancer tissues. C. G. L. W.

**Mueller, J. H. Observations on bacterial metabolism.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **18**, 14.

By boiling a meat infusion with 'Norit', a commercial decolorizing wood charcoal, it will be found that the medium which was capable of growing haemolytic streptococci no longer supports growth. By adding 1 per cent. peptone to the treated medium growth again ensues. The substance in question which is removed by the charcoal, is precipitated by mercuric sulphate. The chemical nature of the substance has not been determined.

C. G. L. W.

**Churchman, J. W. The cause of the parallelism between the Gram reaction and the gentian violet reaction. The isolation of gentian positive individuals from a suspension of a gentian negative organism (*B. coli*). Relation of gentian violet reaction to dilution of implanted suspension. The effect of repeated re-inoculations of gentian violet agar with gentian positive organisms. The selective action of gentian violet in relation to chemotherapy. The communal activity of bacteria.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **18**, 17.

The above six communications form an interesting study of the separation of a strain which is usually looked upon as homogeneous within fairly narrow limits. In the first paper it is shown that those organisms which are Gram-positive do not grow in agar containing the dye. To this rule there are about 10 per cent. of exceptions. An attempt was made to train *B. subtilis* to grow in media containing progressively increasing quantities of the dye. This was unsuccessful. With a Gram-negative organism (*B. coli*) an unexpected result was obtained. By stroking a thick suspension of this organism across a divided gentian violet plate, the growth was equally profuse on each side. If, on the other hand, a dilute suspension was employed, the colonies on the gentian violet side became progressively fewer with increasing dilution. Therefore, in a suspension of a Gram-negative organism, only a small proportion of the individuals are gentian negative. It is possible to isolate the gentian positive organisms, and these are found to be perfectly Gram-negative. By cultivating the various colonies on the plain side of a divided plate it is possible to isolate from a gentian negative strain (*B. coli*) a gentian positive strain. There may exist within a single bacterial strain, two types of individuals which, though in every other characteristic identical, are quite dissimilar in their reaction to gentian violet. These types retain the differential characteristic after many transplantations. Further, if a colony which has grown on the gentian violet side of the plate be cultivated and re-implanted on a divided plate, far fewer colonies appear on the dyed side. The reason for this is not clear. It may be due to some sort of communal property, which enables bacteria, instead of pursuing individual careers, to aid each other in their growth and thus accomplish in large groups what they cannot accomplish singly. By repeated re-inoculation of a gentian violet plate with a Gram-positive organism, growth will take place, which did not occur in the earlier inoculations. Bacteriostasis is therefore a complex process, and any attempt to transfer the selective action of a dye on bacteria as found in laboratory trials to general therapeutics should take into consideration the effect of mass of bacteria on the dye. A strain of *B. coli* was isolated which was entirely fast to gentian violet and in large transplantations grew perfectly. Individual cells isolated by Barbour's method never grew. This would indicate that bacteria do not act as isolated individuals. They possess the power, in numbers, of accomplishing effects which, alone, they are incapable of. The nature of this community of action is at present impossible even to guess at.

C. G. L. W.

## RADIOLOGY AND ELECTROLOGY

### *Radio-diagnosis.*

**Sessa, P.** Contributo allo studio roentgenologico dei caleoli biliari. [**Contribution to the study of gall-stones by X-rays.**] *Radiol. med.*, 1920, **7**, 345.

It is due to the study and research of English and American radiologists that our knowledge of biliary calculi and affections of the gall-bladder has increased and become more assured. Having described in detail his method and technique, the author discusses fully the difficulties of seeing the shadows of biliary calculi owing to their transparency to rays, and speaks of the differential diagnostic points. Two views, anterior and posterior, are essential, and a lateral is very useful. Those who have tried the gas insufflation method give varying opinions of its value. Many cases and illustrations are given. The interesting point emerges that with similar technique, apparatus as efficient and powerful as used by the English and American workers, and plates as sensitive, the Italian radiologists do not see as many gall-stone shadows as the former. The author has a percentage of positive results of 10 to 12, which is little above that of his Italian colleagues, but this does not compare with the figures of Knox, &c. The suggested explanation of this difference is that of racial difference in the patients, or perhaps difference in their food, so that the gall-stones are either not produced or are of more transparent composition, though the author does not advance this as more than a tentative suggestion.

N. H. M. B.

**Campo, G.** Les méthodes modernes pour diagnostiquer le cancer de l'estomac. [**Modern methods of diagnosis of cancer of the stomach.**] *Arch. de enfermedados del aparato digestivo,* Vol. 2. (*J. de radiol. et d'électrol.*, 1920, **4**, 473.

Of all modern methods employed for the diagnosis of cancer of the stomach, examination by X-rays and examination of the faeces give the most convincing results.

Of the two radiological processes, radioscopy is superior to radiography because it permits movements of the organ to be observed. Nevertheless the photographic plate is often useful because it registers details too minute to be recognized at sight on the screen. Therefore, in difficult cases, one or two radiographs should be taken in spite of a previous radioscopic examination having been made. If a tumour exist anywhere in the gastric mucosa, it modifies the shape of the organ by pressure on the mucous surface; either an anomaly of the contour of the stomach is observed, or a light zone on the dark base, according as the neoplasm is situated at the side of the organ or entirely on its walls. In the second case the tumour is more difficult to recognize; in the first, normal obscurity is interrupted at the point corresponding to the lesion and the space between the zone that one sees and the zone which one should see, appears irregular and indented. In certain cases a normal image is found, but of a very reduced size, indicating total scirrhous infiltration: in other cases, the neoplasm, being less prominent, does not greatly distort the image of the stomach, but rigidity of the wall and interruption of the peristaltic movements are noticeable at this point.

The commonest seat of gastric cancer is the pyloric region; in most cases, the horizontal part of this region is invisible, because the retraction is such that the very thin line of opaque salt which passes through the stomach to the duodenum is not appreciable, either on the screen or on the plate; it is not rare, in cases of hard growths, to see the gastro-duodenal orifice constantly open, and the opaque meal passing immediately from the stomach to the intestine. This accelerated evacuation may, however, exist in non-malignant cases. In other cases there is true stenosis with a characteristic image of dilatation.

It is also possible that an advanced pyloric tumour may be invisible; this occurs particularly when there is enormous dilatation produced by ulcerated stenosis of the pylorus which existed before the cancer or was provoked by it; a bilocular stomach may also be found. This form of cancer is distinguished from the benign form of ulcer by the irregularity and indentations of the retracted zone.

Hartext has shown, with the help of X-rays, the existence of cancer in 14 per cent. of cases in which it could not be diagnosed by palpation. Reichel quotes 22 cases in which diagnosis was made solely by this method. Rosanoff considers it to be of extraordinary value in early diagnosis.

Of 172 cases examined by the author, 166 were directly visible by radioscopy; 6 were not visible; in 93 the tumour was more or less appreciable by palpation; in 24 only resistance to palpation was noted; and, in 55 cases, neither tumour nor resistance was apparent.

Without denying the immense importance of radioscopic examination, the author does not consider it to be of sufficient value to justify the exclusion of other means of investigation; but it is a valuable method of diagnosis and is often sufficient by itself. Examination must be repeated several times if the result be negative or if it disagree with other signs or suspicions. It is, moreover, a method to be employed carefully so as to exclude any causes of error. S. U. L.-B.

## *Radiobiology*

**Mottram, J. C. The red cell content of those handling radium for therapeutic purposes.** *Arch. Radiol. & Electroth.*, 1920, **25**, 194.

The cases were divided into (1) clinical and laboratory workers, and (2) porters, clerks, &c., in the building. The former show a diminution in the red cells, and a colour index about 1·2; the latter a smaller diminution and a colour index about 1·0. In three cases death followed a profound anaemia: in these the blood-picture was that of an aplastic anaemia. In all cases there was a marked polynuclear leucopenia and absence of signs of regeneration. From these facts it is seen that the workers suffer seriously and need all possible protection. P. L.-B.

**Mottram, J. C. Histological changes in the bone marrow of rats exposed to the $\gamma$ radiations from radium.** *Arch. Radiol. & Electroth.*, 1920, **25**, 197.

Exposures varied from 12–460 hours: if over 48 hours the exposure was carried out intermittently for 12 hours at night. A 12 hours' exposure was equal to $\frac{1}{600}$th of a rad. Radiated specimens showed a diminution in numbers of young and darkly-staining nuclei and of nuclei in the anaphase: also a diminution in the number of mitoses. Penetrating gamma-rays can apparently reach the bone marrow, whereas the comparatively soft X-rays cannot. P. L.-B.

**Milani, E.** Azione antibatterica dei raggi secondari dei metalli colloidali. [**Bactericidal action of secondary rays from colloidal metals.**] *Radiol. med.*, 1920, **7**, 302.

The secondary rays must have a great importance in radiotherapy, but their action has not properly been studied except in the series of experiments made in Rome under the guidance of Prof. Ghilarducci during the last few years. These have been based on his theory of the relation between wave length of rays and specific irritability of individual cells. In the secondary or characteristic rays we have a scale of radiations with an immense variety of wave lengths, which provides a means of studying the specificity of their actions.

The present experiments were designed to test this activity in its influence on bacteria, the source of secondary rays being colloidal preparations of metals and the bacilli *B. prodigiosus.*

(1) The colloidal preparation was held near to, but not in contact with, the bacilli and irradiated.

(2) The colloid was added to the agar on the plate and the strips of sown bacilli thereby irradiated.

(3) The colloid was added to a broth culture and, after irradiation, the mixture was plated.

(4) The colloid was mixed with an emulsion of bacilli and the suspension was irradiated and then plated.

The results were generally negative from the bactericidal point of view when the secondary rays were from colloidal metals held close to or added to the agar of the plate. When the colloid was added to a broth-culture, or when the colloid and the suspension of bacilli were mixed, there was a slight action in the form of delayed growth and altered staining.

In immediate contact with colloidal copper the bactericidal action was more marked. It was first generated by rays of 13–14 W., and increased with diminution of hardness of primary rays to 9 W.

In the fourth series the development of the bacilli was completely and regularly prevented. With gold, silver, and palladium, at 13–9 W., smaller degrees of bactericidal action were seen. Complete arrest of growth could not be obtained even by prolonging the duration of exposure.

Having discussed the nature of the rays given off by irradiated metals—characteristic, scattered, and corpuscular—the author considers their bearing on the interpretation of his experiments. The bactericidal action was ascribable to very soft rays only. On the other hand, a certain action was produced by rays of varying hardness acting on copper, but the maximum effect—arrested development—was obtained only by using primary rays of 9 W. The partial results with the heavy metals may be due to beta rays.

These experiments have a practical value because the future of therapy depends on the understanding of the problems of the possibility of giving to each tissue rays of the appropriate wave length for its individual reaction.

N. H. M. B.

### *Radiotherapy*

**MÉNARD.** Trois cas de grossesse après radiothérapie pour fibrome. [**Three cases of pregnancy after radiotherapy for fibroid.**] *Bull. et mém. Soc. de chir. de Par.*, 1920, Feb. (*Arch. d'électric. méd.*, 1920, **28**, 219.)

The author declares it to be impossible to give a scientific explanation of the action of X-rays on fibroids. Certain fibroids do not decrease in size, while others completely disappear. He does not systematically seek the menopause, as does Béclère. In certain cases that he has had under observation a simple course of irradiation of the uterine mass caused the haemorrhage to cease.

(1) The patient, 42, had had four normal pregnancies. In 1915 the periods became more abundant, from March 1916 she was never more than eight days in the month without losing. Fourteen séances of radiotherapy were held at intervals of from three to six days. The patient became pregnant after six séances and the confinement was normal.

(2) The patient, 33, began treatment in October 1916. After seven séances the periods became normal and lasted four days, then ceased. Radiotherapy was continued, one séance per fortnight. In March she was stated to be pregnant. The confinement took place normally in July 1917. Pregnancy began when the uterus had been irradiated seven times, and the eleven following séances did not interrupt it.

(3) The patient, 32, began treatment in September 1918, and continued it at the rate of one séance per week. After 29 séances the periods were normal and then ceased. In all, 39 séances were held, and in September 1919 the patient was stated to be pregnant. Pregnancy began after 29 irradiations and six further séances were given. The confinement was expected in March 1920.

Ménard thinks that it is necessary to irradiate the uterus while protecting the ovaries, although in certain cases the haemorrhage can only be stopped by irradiation of the ovaries.

These three observations prove that it is often possible to save at least one ovary, since the three patients became pregnant, and in the first two, who came to term, menstruation reappeared at the usual interval after parturition. S. U. L.-B.

**MARTINDALE, L. Intensive X-ray therapy versus hysterectomy for fibromyomata of the uterus.**] *Arch. Radiol. & Electroth.*, 1920, **25**, 97.

In 39 per cent. of cases radiotherapy was the treatment.

The technique is that used at the gynaecological clinic of the Freiburg University with slight modifications, due chiefly to the adoption of the Coolidge tube. Cross-fire is employed through 20–22 ports of entry, through 18 ports over the abdomen, and 2 or 4 over the sacrum. The distance between the anticathode and the skin is about 18 cm. The exposure is three minutes for each area with a Coolidge tube with hardness 8 and 4 milliamps: this is done on two consecutive days.

Physical signs and symptoms determine treatment as far as possible: if the tumour were not larger than a six months pregnancy, were interstitial, and menorrhagia the prominent symptom, X-ray was chosen. If the patient could not undergo an operation, by reason of her health or occupation, X-ray was used. If the fibroid were small and causing no symptoms, no treatment was undertaken.

In most cases there are no unpleasant effects.

In all cases of doubtful diagnosis, an exploratory laparotomy followed by hysterectomy if necessary is the best treatment. P. L.-B.

## *Radium Therapy.*

**PINCH, A. E. H. A report of the work carried out at the Radium Institute, London, from Jan. 1, 1919 to Dec. 31, 1919.**

**Malignant Conditions.** Malignant growths vary somewhat in their susceptibility to radium according to their nature. If $D = Q \times T$ when $D$ is the dosage in milligramme-hours, $Q$ is the amount of Ra bromide in milligrammes, and $T$ is the length of exposure in hours, in general terms epiblastic growths are more favourably influenced when $Q$ is relatively low and $T$ high; hypoblastic growths when $Q$ is high and $T$ low; and mesoblastic growths are in an intermediate position.

Except in cases of rodent ulcer all the cases are inoperable.

*Carcinoma of the breast.* In the encephaloid type the prognosis is invariably bad. Prolonged screened exposures to the periphery occasionally retard the progress of the disease. The atrophic type usually responds well to prolonged screen exposures.

If the skin be ulcerated healing may often be induced by 12–18 hours exposure with 'half strength' applicators with 1 mm. silver screens.

Small isolated nodules are best treated by inserting an emanation tube with 1 mm. silver screen from 18–24 hours. Prolonged screened exposures are necessary for metastases in liver, lung, &c.

*Carcinoma of the uterus.* In a few cases patients are treated to diminish fixation and aid subsequent operation. Radium treatment appears to exert a very beneficial effect upon carcinoma of the cervix.

In inoperable cases, definite benefit nearly always results, and the progress of the disease is greatly retarded.

The most favourable cases are patients over 50 years of age with little fungation and fixation; but dissemination is always likely to occur.

Recurrences in the vaginal wall often do well if taken early.

In cases of cervical carcinoma of the cauliflower type, as much of the growth should be removed as possible: a tube of not less than 100 mg. of radium should be inserted with a screen of 1 mm. of silver or 2 mm. of lead. A silver screen in contact with the vaginal wall for more than 18 hours is likely to produce a fistula, but within the cervical canal this is not likely to occur. The exposure should be 20–24 hours and may be supplemented by a plate of 100 mg. or more of radium with a 2 mm. lead screen over the fundus. Exposures should be repeated in not less than six weeks. Small emanation tubes of 20–30 mg. initial activity with 0·3 mm. platinum screen may be inserted into circumscribed nodules in the cervix for 12–18 hours.

*Carcinoma of the body of the uterus.* Hysterectomy should always be performed if possible. If radium is used, a tube of not less than 100 mg. with a 1 mm. silver screen should be inserted into the uterine cavity, and a plate of equal strength with 2 mm. lead screen, applied over the fundus.

*Carcinoma of the tongue, palate, buccal and pharyngeal mucous membranes.* As a whole they do not respond well. For prognosis they are divided into two groups: (1) Those in which acute ulceration predominates. (2) Those in which induration predominates. The first class do badly; the second class respond better; when the induration is circumscribed the insertion of a tiny powerful emanation tube with 0·3 platinum screen for 5–6 hours brings about disappearance. Radiation of the cervical and submental glands should be carried out as a prophylactic measure.

Exuberant papillated growths on the buccal mucous membrane, if taken early, often clear up entirely by the insertion of powerful emanation tubes.

Prolonged screened exposures in cases of long standing lymphatic infection with fixed and hard glands often considerably diminish the size of the glands and prevent ulceration of the skin over them.

*Carcinoma of the rectum.* Healthy rectal tissue is very susceptible to radium rays, especially in men. The most suitable growths are annular and situated in the upper half of the rectum: if the radium be placed in the lumen of the gut no proctitis is set up. In the plaque-like type of growth some proctitis almost invariably occurs. If there be extensive ulceration a preliminary colostomy should be performed.

The routine treatment is the insertion of a tube of 100–200 mg. with a 2 mm. lead screen for 15–30 hours: the dose should not exceed 3,000 mg.-hours, and the exposure should not be repeated in less than two months. Healthy mucous membrane must be protected.

*Rodent ulcer.* For this type of case radium is to be preferred to any other form of treatment in an untreated ulcer of recent origin. Lesions up to 3 cm. in diameter and not affecting bone or mucous membrane are almost invariably removed by one application of from 1½–3 hours with a 'full strength' applicator unscreened. Treatment must be carried out well beyond the edge of the lesion. The hypertrophic type will take a larger dose than the ulcerative: with the latter it is advisable to give a larger dose to the borders of the growth.

When affecting the palpebral mucosa, a rodent ulcer can usually be eradicated by radium, but when the ocular conjunctiva is attacked the prognosis is not nearly so good.

Rodent ulcers that have been previously treated with $CO_2$, scraping, &c., need careful treatment owing to the devitalized condition of the tissues. A prolonged exposure of 24–30 hours with a half-strength applicator and 2 mm. lead screen gives the best results.

If bone has been attacked the affected portions should be removed before commencing radium treatment.

*Carcinoma of the bladder.* Treatment often gives good results, especially in females, both because of the easier introduction into the bladder and because a screened tube can be inserted in the vagina in apposition with the trigone. A few cases of epithelioma of the female urethra have also been satisfactorily treated by the combined method.

*Carcinoma of the prostate.* If the disease be localized to one lobe a screened silver tube should be buried in the mass, or a tube of 100 mg. activity, with 1 mm. silver screen, is placed in the penultimate section of a bicoudé catheter which is introduced for 2 hours on five successive days. This may be supplemented by an exposure over the perineum and also by a tube introduced per rectum.

*Carcinoma of the oesophagus.* Definite, but only temporary relief may be obtained: treatment should be carried out by a laryngologist. An emanation tube of not less than 100 mg. activity with a 1 mm. silver screen should be used for 15–20 hours. Treatment must be continually repeated.

*Carcinoma of the stomach and intestines.* Prolonged exposures with heavily screened applicators sometimes diminish pain and arrest the progress of the disease.

*Sarcomata.* Periosteal usually respond better than endosteal; myelomata vary. Spindle-celled varieties respond best, round-celled not so favourably, the large round-celled are intermediate. In melanotic sarcomata the primary growth may often disappear, but ultimately metastases appear.

Sarcomata of the nasopharynx often disappear within a month of treatment. Lympho-sarcomata attacking the cervical and mediastinal glands usually show a marked improvement for a time, but repeated exposures are needed at intervals for 3–4 years. Ultimately the disease gains the upper hand.

*Endotheliomata.* Most frequently seen as a parotid tumour; radium treatment is often of value in inoperable cases. Unless all parotid substance has been previously removed, prolonged irradiation with heavily screened apparatus applied externally should be used.

**Non-malignant conditions.** In cases of uterine fibroids, treatment with radium is very beneficial. The best method is to introduce a 100 mg. tube with 2 mm. lead screen into the uterine cavity combined with applicators of from 100–200 mg. similarly screened applied above the pubes for 24–30 hours. Treatment should be repeated. There may be a premature menopause. The treatment of chronic metritis is the same.

*Naevi.* Treatment of cavernous naevi gives excellent results if taken early. ‘Half strength’ applicators with 0·1 mm. lead screen should be used, employing cross-fire. Exposure, 30–60 mins. on three successive days, at about 6 weeks intervals.

Results in cases of capillary naevi vary; idiosyncrasy is great. Not more than 15 mins. exposure with a ‘half strength’ applicator at first; later, exposures of 1–1½ hours with 0·1 mm. lead screen. There is always a tendency to the appearance of telangiectasis.

*Corns, warts, papillomata, and keratomata* can be removed by exposures of 1–1½ hours with ‘full strength’ applicators unscreened. Tendency to recur is slight.

*Keloids and vicious cicatrices.* Radium treatment is better than surgical: early treatment is essential. ‘Half strength’ applicators with 1 mm. silver screen for 6 hours on 3 successive days.

*Lupus erythematosus.* Often greatly improved. ‘Half strength’ applicators unscreened for 30–60 mins. at intervals of 4–6 weeks should be used. Treatment should be carried well beyond the borders of the lesions.

*Tuberculosis.* (a) *Lupus vulgaris of skin.* If Finsen light fails, radium often gives good results, especially when the mucous membrane of the nose is affected. Tubes of 25–50 mg. with 1 mm. silver screen are applied inside the nose with a ‘full strength’ applicator with 2 mm. lead screen applied externally; exposure 6 hours. In ordinary skin lesions screened and unscreened tubes are necessary, the former for indurated and the latter for ulcerated areas.

(b) *Lupus vulgaris of palate and fauces.* 'Full strength' unscreened apparatus for 30–60 minutes is generally followed by healthy scar tissue.

(c) *Tuberculous adenitis.* When the cervical triangles are affected prolonged exposures with heavily screened applicators are recommended. Pigmentation is very liable to occur.

*Exophthalmic goitre.* In early stages radium does good. Prolonged screened treatment with 200–300 mg. is used. The first effect may be an exacerbation of all symptoms for 2–3 weeks. In advanced cases great caution is needed.

*Leucocythaemia.* (a) *Splenic.* Radium treatment is advisable as a preliminary to operation. An exposure of 24–30 hours with 400–500 mg. screened with 2 mm. of lead should be employed.

(b) *Lymphatic.* Radium treatment may improve the blood condition and general health for a time.

*Skin diseases.* Radium does good in many chronic superficial diseases. 'Half or quarter strength' unscreened applicators are employed for 3–15 mins. every 2–3 weeks.

*Arthritis deformans.* Recent cases of a peri-articular type are often benefited by the daily administration of 500 c.c. of radium emanation solution of a strength not less than 1·5 mc. per litre.

**Report of the Chemico-Physical Laboratory.** In preparing emanation applicators certain precautions should be taken: (1) Strong fans should be installed to prevent the inhalation of air diluted with emanation. (2) Rubber gloves should be worn when working with mercury. (3) All tubes, &c., containing radium, should be kept as far from human beings as possible when not in use.

A comparison of the various radium salts shows that only the sulphate gives an efficient and permanent result. The explosion of tubes containing radium salts is considered to be due to incomplete dehydration of the salt.

**Report of the Research Department.** The first communication dealt with the great and rapid leucopenia produced by exposure to radiation and the comparatively slow return to the normal when the worker is removed from the influence of the radium. The second communication dealt with ultra-violet radiation. Patients showing a spotty appearance under ultra-violet radiation appear to be more susceptible to radium radiation than those who are relatively unspotted. P. L.-B.

## *Electrotherapy*

**DE KRAFT, F.** Action des courants électriques sur les glandes à sécrétions internes et les autres tissus. [**Action of electric currents on the endocrine glands and on other tissues.**] *Med. Rec.*, 1920, Jan., 136. (*J. de radiol. et d'électrol.*, 1920, **4**, 431.)

High frequency currents in general application excite nutrition, destroy toxins, augment the excretion of $CO_2$, increase the solid residue of the urine, improve the nutrition of the skin, the hair, the nails, &c. In the form of diathermy they warm the blood and the tissues and dilate the capillaries; engorgement of the internal organs becomes less, and these are placed in a condition of better nutrition. At the same time the internal secretion glands become more active; the most common proof of this being increased menstrual haemorrhage in the case of a woman. The author thinks the secretion may be regulated; strong local applications of diathermy on the region of the implicated gland will prevent secretion, and small applications will excite it.

He recommends effluvation for obtaining muscular contractions; a Tesla coil is joined up with an Oudin resonator; one pole is placed upon the patient in the form of a large plate, the other is moved about all over the body. Thus is obtained a better muscular tone, a greater sensation of well-being, and a possible decrease in weight of 50 lb. in 60 séances.

In cases of obesity with disorder of the peripheral circulation, cardiac weakness, enlargement of the abdomen, diminution of urine, the wave current of the static apparatus applied to the abdomen, produces contractions of striated and unstriated muscles, reduces congestion of the liver, improves digestion, warms the extremities, strengthens the heart, and is able to diminish the weight by 100 lb.

The galvano-faradaic-sinusoidal combination is very useful in diabetes, gout, and in mental and nervous disorders. Applied from the back to the abdomen it tones up the muscles of both, improves the general condition of the body, benefits venous circulation (especially the portal) and lymphatic circulation. Reduction of weight produced by dietetic treatment has the drawback that it predisposes to displacement of the internal organs by causing the disappearance of their fatty support without re-establishing muscular support, while electrotherapy is free from this objection.

S. U. L.-B.

# MEDICAL SCIENCE
## ABSTRACTS & REVIEWS

Volume IV. Number 2 May 1921

## CONTENTS

REVIEWS:

PAGE
INTESTINAL PARASITES . . . . . . . . . . . . . 103
DISEASES OF THE SKIN . . . . . . . . . . . . . 110
DISEASES OF THE SPLEEN . . . . . . . . . . . . . 118
BILIARY SURGERY . . . . . . . . . . . . . . 125
CONGENITAL TORTICOLLIS . . . . . . . . . . . . . 132
INTESTINAL EXCLUSION . . . . . . . . . . . . . 137
THE PHYSIOLOGY OF THE ELEMENTARY NERVOUS SYSTEM: ITS BEARING UPON SOME MODERN NEUROLOGICAL PROBLEMS . 141

ABSTRACTS:

NEUROLOGY . . . . . . . . . . . . . . . . 146
PATHOLOGY AND BACTERIOLOGY . . . . . . . . . . . 152
BIOCHEMISTRY . . . . . . . . . . . . . . . 173
RADIOLOGY . . . . . . . . . . . . . . . . 181

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# REVIEWS

## INTESTINAL PARASITES

McLean states that intestinal parasites are infrequent in New York City children living under good hygienic conditions. In examination by him of 308 stools from children up to 12 years of age he found that only 7, or 2·27 per cent., harboured parasites, viz. *Ascaris lumbricoides* or *Oxyuris vermicularis*. In 4 the presence of parasites was determined by the finding of ova, and in 3 by the presence of the parasites.

Under the name of the tongue sign, Couillaud describes an appearance of the tongue met with in oxyuriasis and ascariasis, and characterized by enlargement of the fungiform papillae which are seen in the form of red points distributed over the margins of the anterior surface and tip of the tongue. According to Couillaud this sign may appear by itself apart from any other symptom of helminthiasis. On expulsion of the worms from the intestine it rapidly diminishes and disappears entirely. While possibly indicating a catarrhal condition of the intestine, the sign is more probably due either to toxaemia or to slight and repeated irritation of the intestinal mucosa with reflex involvement of areas innervated by intermediate bulbar centres.

According to Neumann, who records two cases of oxyuriasis and one of ascariasis in infants, intestinal parasites, while very frequent in older children and adults, are rarely met with in infants. He quotes Israilten, who made investigations in Zurich into the frequency of intestinal parasites in man, and among 994 children examined found only three infants with intestinal parasites.

According to the statistics of Stiles and Garrison which include statistics from the United States, the Philippines, India, West and Central Africa, Italy, England, Russia, and Germany, no entozoa were found in children under one year.

An intestinal parasite which is very rare in Germany, but relatively frequent in infants, is *Taenia cucumerina*. Its frequency in infants is explained by its being transmitted by the dog-flea and the close association so often present between dogs and infants. *Taenia cucumerina* in infants is especially frequent in Denmark, where dogs are very plentiful. Other tapeworms such as *T. flavopunctata*, *T. saginata*, *T. solium* and *Bothriocephalus* are rare in infants, and infestation by *Oxyuris vermicularis* or *Ascaris lumbricoides* is not frequent at this age.

Hoffmann, of the Zurich University Children's Clinic, remarks that much more importance was attached to intestinal parasites, and especially ascarides, by the older writers than at present, all sorts of symptoms being attributed to them, so that it is often difficult to distinguish truth from fiction in the old descriptions. On the other hand, at the present day, there is a tendency to underestimate the significance of these parasites, though it is probable that owing to the progress of hygiene the frequency of these parasites and their complications has to some extent diminished. In districts where ascarides are extremely prevalent, such as the tropics, considerable importance is still attributed to them. In European countries their frequency varies considerably. Thus, whereas, according to Langer, 52 per cent. of the country children in Bohemia are infested with ascarides, the figures in the towns are considerably lower, e. g. 4 per cent. among the children in Prague. Hoffmann has collected 63 cases of intestinal obstruction due to ascarides, including 7 personal cases, 5 of which were in children aged from 1½ to 9 years and 2 in adults aged 20 and 21.

According to von Uji, who reports a case of intestinal obstruction due to ascarides, the occurrence and severity of the obstruction do not bear any relation to the number of the worms. A large number of worms is not by itself sufficient to cause obstruction, but overeating, errors in diet, chill, and strain are predisposing causes. von Uji alludes to severe cases of ileus verminosus collected by Nobécourt, of which three were cured by operation, one died in spite of operation, and three died without operation. The diagnosis is decidedly difficult, and in most cases the condition is not discovered until autopsy or laparotomy.

According to Crowell, who records his experiences of the parasite in the autopsy room during several years in Manila, *Ascaris lumbricoides* is more widely distributed geographically, and infests a larger number of persons, than any other known intestinal parasite. Its pathological effects are classified by Crowell as follows: (1) Mechanical effects may be caused by the worm in the intestine or in the course of its migrations to the bile-ducts, liver, pancreas, stomach, oesophagus, accessory nasal sinuses, lacrymal duct, Eustachian tube, external ear, larynx, and trachea; (2) the worm is also of importance as a carrier of infection in its migrations to the peritoneum, liver, gall-bladder, and pancreas; (3) the larvae cause broncho-pneumonia in experimental animals, and it is not improbable that they may do so in some cases in infants; (4) the presence of a harmful toxic substance is a source of danger, and reflex nervous symptoms, due either to mechanical or toxic irritation, are also frequently encountered.

Eberle of Offenbach, states that though over 100 cases of invasion of the bile-ducts by ascarides have been published, invasion of the pancreas by these parasites is very rare and usually occurs *post mortem*. Vierordt's case, published in 1904, was the first in which a definite diagnosis was made during life, well-marked lesions being found in the pancreas at the autopsy. Eberle's case, which is the third on record, occurred in a woman aged 45, from whom 31 ascarides were removed at the operation from the bile-ducts, and 35 at the autopsy, five hours after death, from the liver, pancreas, and pancreatic duct, as well as from the oesophagus, stomach, and intestine. She also presented the very rare association of gall-stones and worms, only three examples of which have been collected by Neugebauer.

According to Ransom, chief of the Zoological Division of the United States Bureau of Animal Industry, recent investigations on *Ascaris lumbricoides* have shown that after the young worms hatch in the intestine they do not immediately settle down, but migrate to the liver, lungs, and other organs, meanwhile undergoing considerable growth and development. Those that reach the lungs return to the intestine by way of the trachea and oesophagus, then settle down and develop to maturity in a suitable host (man, pig); otherwise they are soon eliminated in the faeces (rat, mouse, guinea-pig, rabbit), or in some hosts undergo an abortive development that falls short of fertile maturity.

Mosler, in 1867, and Lutz, in 1868, recorded the occurrence of pulmonary symptoms in human beings following experimental administration of ascaris eggs, the symptoms being very probably due to invasion of the lungs by the migrating ascaris larvae. Ransom urges that the question of the occurrence of pulmonary symptoms in human beings as a result of ascaris infection should receive careful attention, especially in the case of young children.

Bourges records a case of acquired haemolytic jaundice which occurred in a young soldier infested with *Ascaris lumbricoides.* The symptoms gradually disappeared in the course of two months after expulsion of 29 ascarides by santonin. All other causes of haemolytic jaundice, such as syphilis, tuberculosis, and malaria, could be excluded, and there was no evidence of gastric cancer, cirrhosis of the liver, or myeloid leukaemia. Bourges therefore concludes that the haemolytic icterus in this case was due to the action of the ascarides on the red corpuscles. He alludes to a similar case of haemolytic jaundice reported by Darré, which appeared in the course of ankylostomiasis and was cured after treatment with thymol.

Läwen and Reinhardt examined 620 appendices which had been removed at St. George's Hospital, Hamburg, since the spring of 1914, and found oxyurides present in 60 cases, or 9·76 per cent. The worms were found twice as frequently in the female as in the male appendix. 12 of the affected appendices occurred in children up to the age of 14, and 48 in adults. The oldest patients were aged 42, 43, 46, and 62 years, and were all women. In all but 7 cases, in which the operation showed abdominal lesions such as tubal pregnancy, cholecystitis, tuberculosis, &c., in addition to the presence of oxyurides in the appendix, the clinical picture was that of a mild, moderate, or, in rare cases, a severe attack of appendicitis. The condition is attributed by Läwen and Reinhardt to the oxyurides penetrating the mucous membrane and so opening up the path for a bacterial infection. It is probable also that the toxic action of the parasites causes a superficial transient inflammation of the mucous membrane. Clinically, a certain diagnosis cannot be made, but relatively slight objective findings, combined with fairly acute or chronic symptoms, is suggestive of oxyuris appendicitis. This diagnosis will be all the more probable if oxyurides have already been found in the stools several years previously. On opening the abdomen an abundant serous effusion is sometimes a sign of oxyuris appendicitis, but frequently the effusion is confined to the serous coat of the appendix.

Fürbringer of Berlin, regards the war as mainly responsible for the unusual prevalence of the *Oxyuris vermicularis* both among children and adults within recent years. Whereas, previously, oxyurides were usually transmitted from children to adults, during the war the young civilian population had the disease transmitted to them by soldiers home on leave in whom infestation had been favoured by life in the trenches and barracks. The change in the character of the food, with the predominance of a vegetarian diet, also helped to explain the unusual frequency of oxyuriasis.

Mayer records the results of the examination of the stools or blood, or both, of coloured prisoners in the prisoners' camp at Wünsdorf in 1917. The most striking finding was the prevalence of hookworm infection, especially among the West Africans (56 per cent.) and the Indians, particularly the Ghurkhas (62·7 per cent.), in marked contrast with the low percentage of hookworm infection among North African prisoners (2·1 per cent. among 239 examined).

In response to representations made by the International Health Commission of the Rockefeller Institute, the Indian Research Fund Association have devoted a considerable amount of attention to the subject of ankylostomiasis in India. The first inquiry started under their auspices was conducted by Lane among the labour forces employed in the tea gardens in the Darjeeling districts, 66·02 per cent. of whom were found to be infected with *Necator americanus.*

Mhaskar, officer in charge of the ankylostomiasis inquiry in Madras, reports that the percentage of hookworm infection is nearly 100 in the four districts of Tanjore, Trichinopoly, Madura, and Ramnad. Of the two species of hookworm harboured—*Necator americanus* and *Ankylostoma duodenale*—the percentage of the former is nearly 100, while that of the latter varies widely, being 80 per cent. in Tanjore and 10 per cent. in the Madura district. Hookworm infection, though universal, was found to vary in intensity in the various districts in communities. Freedom from hookworm infection appeared to diminish the susceptibility to bowel complaints.

Megaw, professor of pathology at King George's Medical College, Lucknow, states that hookworm infection is exceedingly prevalent in the United Provinces, and that nearly every one there who reaches adult life harbours hookworms, or has at some time harboured them. Not only does hookworm infection cause many deaths every year, but it produces some degree of mental and physical deterioration in an enormous number of individuals. In the aggregate there is a very great economic loss to the provinces.

Caius and Mhaskar have written a series of papers, in connexion with the hookworm inquiry in the Madras Presidency, on the correlation between the chemical composition of anthelmintics and their therapeutic values. Their principal conclusions were as follows: (1) Thymol is a powerful vermicide acting both on *Ankylostoma* and *Necator.* Any dose from 30 to 60 grains in one portion will prove effective. Thymol has mild vermifugal properties. As its use does not interfere with the daily occupations of the individual, it is likely to find favour with the masses. (2) *Ol. chenopodii, ol. absinthii, ol. tanaceti,* and *ol. cajuputi* are all more or less toxic, and cannot be recommended as anthelmintics.

Waite and Neilson report that during 1918 the State of Queensland, the Australian Institute of Tropical Medicine, and the International Health Board of the Rockefeller Foundation conducted jointly a hookworm inquiry in North Queensland, and found by stool microscopy 21 per cent. of the the total population infected. From examination of 340 children, Waite and Neilson found that hookworm disease produced mental sluggishness and retarded mental development according to the massiveness of the infestation. Prolonged hookworm infestation appeared to produce cumulative mental retardation.

Schapiro, state director of the campaign for the relief and control of hookworm disease in Costa Rica, states that there is a permanent increase in haemoglobin as the result of treatment, which is also followed by an increase in earning capacity, and increase in acreage cultivated, and a marked reduction in morbidity and infantile mortality.

According to Brosius and Bishop, hookworm disease is almost universal among the natives of the district of Zaragoza, Colombia, 98 per cent. of the inhabitants being affected. All forms of intestinal parasites live and thrive in the same individual, no type producing conditions inimical to the life of the others. The writers came to the conclusion that the normal haemoglobin value of the blood in the natives of this region is somewhat lower than in temperate zones, viz. about 70 per cent. In the hookworm infested population of Zaragoza the average haemoglobin percentage is 47, but an immediate rise, varying from 20 to 50 per cent., follows expulsion of the worms from the patient's intestine.

Darling, professor of hygiene in the São Paulo Faculty of Medicine, describes the work done in the Far East by the Malaya Board on the treatment of hookworm infection. The Board discovered that hookworm infection existed to a greater extent in the tropical east than was generally recognized, practically 100 per cent. of the agriculturists, who form the great bulk of the population, being infected. It was shown that there was a correspondence between the degree of infection—that is, the actual number of worms harboured—and the amount of blood loss or anaemia suffered. A given number of worms produced more anaemia among children than among an equal number of women, and more anaemia among women than among an equal number of men. It was estimated that about 12 hookworms were required to cause a loss of 1 per cent. haemoglobin. When the number of worms harboured was considerable, the anaemia caused was evident and measurable; when only a few worms were harboured the blood loss might not be detectable.

Darling states that the Malaya Board found that chenopodium was more effective than thymol in killing hookworm, and that it was even more efficacious in expelling ascaris and other helminths such as oxyuris, trichiurus, and trematodes. The dose of 1·5 c.c. oil of chenopodium was highly efficient and but slightly toxic, sometimes causing transient dizziness and vomiting.

Smillie of São Paulo, found that large doses of betanaphthol (18 grm. for adults), which he used in the treatment of 79 cases of hookworm disease, caused very severe toxic symptoms in two cases and also produced marked changes in the blood-cells in two other cases. The drug caused considerable destruction of the red corpuscles, with resultant severe anaemia, icterus, enlargement of the spleen, liver, and gall-bladder, and haemoglobinuria. The leucocytes were apparently not destroyed by the drug. Smillie concludes that betanaphthol in large doses is so toxic that it cannot be recommended for general use in the treatment of hookworm disease.

As the human habitat of the hookworm is the first portion of the duodenum with extension along the intestine in both directions in the severer infections, Kantor, gastro-enterologist to U.S. Army General Hospital, No. 14, has devised an intra-intestinal tube treatment which he claims to be more efficacious, safer, and, once the duodenal bucket is in place, quicker than the methods at present in vogue. After introduction of the duodenal tube, 2–3 c.c. of oil of chenopodium are injected through it, and, after an interval of six minutes to allow the oil to diffuse through the worm-bearing area, 2–3 oz. of a saturated solution of magnesium sulphate are injected to prevent toxic absorption of the oil.

Moog and Wörner, of the Frankfort University Medical Clinic, allude to the prevalence of the *Tricocephalus trichiurus* in soldiers (vide *Medical*

*Science*, 1920, **1**, 402), and report their investigations as to its incidence among non-combatants. As compared with a frequency of 46 per cent. among soldiers, the stools of 200 non-combatants showed the ova of *Trichocephalus trichiurus* in 66, or 33 per cent. In none of the cases could any symptoms be definitely attributed to the presence of worms. The number of ova in the faeces of the non-combatants was very small compared with the enormous amount present in the faeces of soldiers. Eosinophilia was found in only 8 of the 66 parasite carriers and therefore could not be regarded as a constant symptom.

Mouriquand and Bertoye report an example of a syndrome which is little known, viz. trichocephaliasis with severe anaemia and diarrhoea. Such cases may be fatal, but recovery has followed so radical a method as irrigation of the colon with soap and water through an appendicostomy opening. This was successful when all else had failed. The present case, however, proved fatal, and the autopsy revealed myriads of the trichocephalus fixed to the mucous membrane in bunches. No definite haemorrhagic spots were seen. The blood examination showed three million red cells, but only 20 per cent. of haemoglobin, so that the colour index was 0·3—a figure seldom met with. There was an eosinophilia of 11 per cent.

Herzog records a case of bothriocephalus anaemia in which the blood-picture exactly corresponded to that of pernicious anaemia, although all the other symptoms of that condition, especially achylia gastrica and glossitis, were absent. This shows that bothriocephalus anaemia cannot be identified with Biermer's disease. It is obvious that the bone marrow reacts in the same manner to different stimuli just as other tissues do. In Herzog's case there was an extensive pigmentation of the skin which he regarded as haemochromatosis.

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J. D. R.
G. W.

# DISEASES OF THE SKIN

The most important event in the dermatological world during the last six months has been the attainment of his seventieth birthday by the celebrated physician Unna of Hamburg, and the occasion was appropriately commemorated by the publication of a special number, on September 8, of the *Dermatologische Wochenschrift,* the journal which was founded by him in collaboration with Hebra and Lassar under the name of *Monatshefte für praktische Dermatologie* in 1882, and which has ever since largely been supported by him and his numerous followers. The special number reveals his enormous energy and the wonderful variety of aspects under which his genius has manifested itself.

A contribution to the chemistry of the skin of some importance is made by Strauss, who has investigated the composition of keratin. He employs Unna's method of splitting it by the action of sulphuric acid and hydrogen peroxide and dissolving as much as possible of the product with ammonia. The insoluble residue designated Keratin A he finds common to all varieties of keratin. The soluble portion when acidified yields a precipitate Keratin B which varies according to the variety of keratin investigated, e. g. nails, horn, hoofs, hair, &c. Albumoses are also found in the filtrates. There is no reason to believe that the refractory behaviour of keratin is in any way proportional to the amount of sulphur contained in it.

Apart from this there has been nothing of striking moment published on dermatological subjects. Many workers are struggling to solve the still elusive problems presented by the common diseases of the skin. There seems to be an increasing tendency to regard **psoriasis** as an infective disorder. Bory, for example, defends this theory very strongly, he quotes several cases where it has apparently been propagated by contagion, and he also points out that the most successful remedies are parasiticides, associated, it is true, with reducing agents. Lennhoff has attempted inoculation experiments and has inoculated psoriatic subjects with matter from their own lesions, and in about 15 per cent. of his attempts has been successful. Control situations inoculated with scales from the author's own healthy skin did not in any case develop the disease. The majority of people he regards as immune to the disease, and therefore, he did not attempt to inoculate them. Adamson (1) thinks that keratodermia blennorrhagica, which is always associated with gonorrhoeal arthritis, is merely a form of psoriasis. He points out that the psoriasis associated with all forms of arthritis is often of the rupioid type, with scales heaped up into horny cones, while again in many cases of keratodermia blennorrhagica it is detailed that the patient had psoriasis on other parts of the body. In some cases it is difficult to diagnose between the two conditions. He therefore concludes that keratodermia blennorrhagica is merely a special form of psoriasis. The description of a case of this condition by Isaac, in the same number of the *British Journal of Dermatology* as Adamson's paper, certainly supports the latter's theory.

**Eczema.** In America several observers have been trying to establish a relationship between eczema and the sensitization of the skin to certain proteins in the food. Strickler and Goldberg made extracts of proteins from many foods and injected patients with them in the hope of getting reactions in various dermatoses, but their results were indefinite; so were those of White, who also found that 28 patients whose eczema was of the dry variety had an excess of fat in the faeces, while 4 patients with moist eczema had an excess of starch. Ramirez also tested 78 cases of eczema for protein sensitiveness with 30 positive results, and 10 of these were cured by removing the faulty protein from the diet. Nevertheless, he concludes that only a small proportion of eczema cases are anaphylactic. So far this line of research has not yielded striking results, but the Americans are still hopeful. Montgomery and Culver point out that there are several varieties of eczema of the vermilion border of the lips, some of which are serious and may become the starting-point of cancer. They strongly recommend treatment with radium. Galewsky (1) states that many cases of eczema of the forehead are caused by the leather substitutes in hat linings containing nitrocellulose and cresol. Moro writes on sudden death in eczema; he says that it always occurs between February and April, and thinks that the sympathetic nervous system is hypersensitive at this season. He thinks that the external treatment of infantile eczema may be dangerous if too successful. The seasonal variations in various skin diseases are also discussed by Bettmann, but after much deliberation he is only able to arrive at the conclusion that the totality of cosmo-meteorological conditions affect the human organism in the most complicated way.

The constant efforts made to improve the treatment of **chronic sepsis of the skin** are exemplified by Galewsky (2), who writes in praise of 'Staphar', which is a staphylococcic vaccine from which poisonous constituents have been eliminated and which consequently can be given in extremely large doses. It corresponds to the detoxicated vaccines which are now being prepared in Great Britain. Montel recommends the local application of dressings of antistreptococcic serum in cases of erysipelas and lymphangitis, while Becher advocates the use of a 10 per cent. solution of oil of turpentine in olive oil in almost all septic conditions of the skin, also in eczema, buboes, and pruritus. But most observers agree that on the whole the collosol manganese gives as good results as anything in the treatment of obstinate furunculosis.

The whole subject of **lichen** and lichenification has been exhaustively discussed by Dind who upholds the thesis that lichen planus and all its modifications, together with the lichen simplex chronicus of Vidal or neurodermatitis, are the same disease. His arguments are (1) that the histological features in all are of the same character; (2) that both conditions may occur either simultaneously or in succession in the same patient; (3) that in each type the course and characters of the eruption point to a parasitic cause; (4) that both types of lesion are very amenable to treatment with arsenic, especially intravenous injections of arsenobenzol. It may also be mentioned that Bonnet and Morenas advocate large doses of cacodylate of soda in the same conditions. On the other hand Thibierge strongly supports the idea that lichen planus is quite distinct from lichen simplex and its modifications.

**Pigmentation of the skin.** With and Kissmeyer have studied the effect of light baths on patients with vitiligo. They find that at first the vitiligo becomes more visible, but that subsequently a macular pigmentation appears on the patches, which may continue spreading after the light baths have ceased. The vitiligo patches at first react to the light baths with a stronger erythema than the normal skin, but little by little the patients are able to stand a quantity of light to which formerly they reacted with erythema not only upon the normal but also upon the non-pigmented areas of the skin. Consequently they infer that the organism is capable of protecting itself against light in other ways besides pigmentation. Vitiliginous skin does not give the dopa-reaction, but where the new macules of pigmentation occur there is an intense dopa-reaction chiefly in the cubical cells of the basal layer. They regard vitiligo as an exhaustion dermatosis caused by the using up of the dopa-oxydase by some unknown stimulant. Their results support the view that all skin pigment is formed in the epidermis, not in the deeper layers. Wassermann discusses the fact that the soldier's skin often becomes deeply pigmented, especially in the dark. races. He thinks that not only exposure but also the food available on service may contribute towards this. Post-mortem pigmentation of the skin is dealt with by Neubürger. He shows that the human skin darkens after death, especially those parts which are normally inclined to be darker. The cause of death makes no difference unless it be Addison's disease or another condition which augments pigmentation during life. These are succeeded by increased post-mortem pigmentation. The pigmentation is independent of bacteria but needs free oxygen. It is derived from the epidermis and is produced by the oxidation of 'dopa' or dioxyphenylalanin, in life carried out by a ferment in the cells of the basal layer. In fact his results agree with those of With and Kissmeyer.

**Tuberculosis.** Vogel describes a case of tuberculosis cutis vegetans, Cranston Low and Logan publish a fatal case of lupus erythematosus in which tuberculous lesions were found at the autopsy, Kiendl gives a warning against the use of tuberculin in lupus erythematosus and also states that the administration of quinine may be followed by a temporary exacerbation of the eruption, while Adamson (2) writes to point out what excellent results may be obtained in the treatment of lupus vulgaris by the use of that old remedy liquid acid nitrate of mercury, both on the skin and also the mucous membranes, with and without ulceration. His results, which others have since confirmed, make it appear strange that for so long this caustic has been allowed to fall into desuetude.

**Fungoid infections.** Up to recently small-spored ringworm was a rarity in Austria, but it has now been introduced by children returning from western Europe, where they have been boarded out in order that they might escape the terrible economic conditions of Austria. Stein, therefore, has a paper on the differential diagnosis between large- and small-spored ringworm of the scalp. There is nothing very new in it, but it is interesting to note that he recommends perhydrol as having more penetrating power than other drugs. Nathan has studied the production of antibodies in trichophytic infections. His conclusions are indefinite; he states that immunity phenomena occur in these infections and may be demonstrated sometimes, but not with regularity, not only by cutaneous allergy and immunity, but also by the presence of antibodies in the blood. Noiré points out some of the precautions that must be taken in the X-ray therapy of ringworm of the scalp, especially the importance of not having the tube too far away from the scalp. This necessity is often unrecognized.

**Herpes zoster.** Stern reports the case of a highly neurotic man who had a recurrent eruption on his right buttock and occasionally on his lips, also swellings of the glands and an attack of facial paralysis. Probably a case of herpes febrilis. Bacmeister reports a case where the patient apparently infected two other people with herpes zoster by shaking hands with them. This is interesting, in view of recent tendency to associate herpes zoster with varicella.

**Urticaria.** A case of urticaria tuberosa (Willan) is published by Reiche, cured by atophan. Hoffmann discussed the peculiarities of the urticaria produced by flea-bites. Ward points out that acute fevers are often followed by an attack of urticaria.

**Scabies.** Daubit advocates the use of soluble sulphur in the form of the polysulphide of calcium, as being more rapid than the conventional methods. The danger of dermatitis he thinks can be easily avoided. Pozzo publishes a case of 'Norwegian scabies' in a bed-ridden boy afflicted with tuberculosis from which he subsequently died. Dubreuilh describes an epidemic of an infective pruriginous eruption occurring among the Tonkinese and Annamites imported into France during the war. It was characterized by papules, like those of prurigo or strophulus, which on disappearing left a little brown macule. The eruption was mostly upon the lower part of the body and in the lumbar region. It was certainly not scabies. Glandular enlargement was common; no parasites were found. In hospital a cure was rapidly effected by a weak tar and sulphur ointment.

O'Donovan (1) records an interesting outbreak of dermatitis due to handling figs infected with a mite which was identified with *Carpoglyphus passularum*, one of the sarcoptidae, but apparently unrecognized previously in this country as a cause of dermatitis.

**Scleroderma.** A long paper is produced by Adrian and Roederer on affections of the joints in scleroderma, with full consideration of the literature of the subject. The cases are divided into three groups: (1) in which the affection of the joints is primary and succeeded by scleroderma; (2) in which joints and skin are attacked simultaneously; (3) in which the skin is attacked first and subsequently the disease extends to the joints. Cases are almost all in females. There is a close connexion between scleroderma and polyarticular chronic rheumatism and certain anomalous forms of tubercle. The aetiology is completely obscure and no useful therapeutics are known. Nevertheless, in many cases the prognosis is fair. Izar publishes a case of generalized scleroderma so extensive as to threaten the life of the patient, a little girl aged 7, which was completely cured by injections of hypophysin and pituitrin given on alternate days.

**Erythromelalgia.** Kunstmann describes a case of this disease which, owing to obstinate ulceration, had to submit to amputation of a leg, in which no pathological alteration, either of the blood-vessels or nerves, could be found. On the other hand, a patient of Chatellier was more fortunate, for she was cured of the same disease by a single injection of a quarter of a milligramme of adrenalin.

**Pellagra.** Probizer discusses the astonishing fact that during the war pellagra almost disappeared from the Trentino. This shows that it is not caused by misery, want, or psychic disturbances, nor by the *Simulium*. The true cause of the freedom from pellagra was the high cost and difficulty of getting maize. He points out that now that the war is ended it is necessary to enforce the various laws against the sale of diseased maize.

**Alopecia areata.** Sabouraud now supports in an ingenious paper, perhaps somewhat tentatively, the theory that this disease is an abortive form of congenital syphilis.

**Myiasis.** A case of 'creeping disease' occurring in Paris and cured by excision is reported by Darier (1).

**New growths.** Quite a number of papers have been written on these.

Darier (2) records an interesting case of the precancerous dermatosis of Bowen in an old man in whom almost all the skin of the face was affected. The disease ran a rapid course and was quite uninfluenced by X-rays.

Savatard (1) (2) (3) has three communications, one a very interesting one on the early diagnosis of epithelioma of the skin, which is often missed in its initial stages. He also publishes a case of leiomyoma or multiple tumours composed of smooth muscle-cells derived from the arrectores pili and a case of the rare fibroma simplex. Lenormant describes a case of the extraordinary condition known as *cutex verticis gyrata* in which almost the whole scalp was transformed into a thick, fatty and malodorous cap lined with deep furrows. It was greatly improved by operation, and reduced to such dimensions that it could be effectually concealed by a wig.

Darier and Hallé publish an interesting case of a naevus derived from the branchial clefts, containing crypts lined with cylindrical epithelium, which the authors regard as intradermic branchial fistulae, and Audry records the case of a child who presented two tumours of the scalp which contained brain tissue although shut off from the cerebral contents by the closure of the cranial sutures. He calls the condition 'nævo-encéphalome'.

Tar cancer is discussed independently by O'Donovan and Kuntzel, who arrive at very similar conclusions, namely, that the incubation is prolonged, that the commonest site is the scrotum, that the type of growth produced is not very malignant, being late in involving glands, and with very little, if any, inclination to metastasis. Henestenberg records a case of acanthosis nigricans with carcinoma of the internal organs and destruction of the left suprarenal body. Satani records a case of extra-mammary Paget's disease in the axilla, treated surgically. Civatte and Vigne discuss the treatment of the sarcoid of Boeck-Darier by intravenous injection of salvarsan. Although it is amenable to this treatment, they still hold that this sarcoid is tubercular in origin. Degrais and Bellot recommend that X-ray epitheliomata in X-ray workers should be treated with radium. They record three successful cases. Nanta and Baudru describe a case of lymphadenoma associated with severe pruritus, and finally Merk has a fanciful paper in which he ascribes Recklinghausen's disease, adenoma sebaceum, and tuberous sclerosis to infection with some dicotyledonous plant, the ghost of the structure of which he is able to make out in serial sections!

**Cryotherapy.** Lortat-Jacob is not satisfied with the conventional methods of applying carbon dioxide snow to the skin, and advocates the employment of a 'cryocautery', i.e. a vessel tipped with copper, in which the snow is formed into a solid freezing mass with acetone. He claims the advantage of more accurate apposition and more intense freezing effect.

Ravaut and Gallerand advocate the treatment of leukoplacia by carbon dioxide snow; they cured a case thereby. But it is painful when applied to the tongue, although on the buccal mucous membrane it is excellent.

**Electrotherapy.** Tomkinson recommends screened doses of X-rays in the treatment of Oriental sore, and thinks that the unsatisfactory results sometimes obtained in this disease may be due to the use of unfiltered rays. Eitner recommends for the electrolysis treatment of hypertrichosis the very fine wires used to preserve the lumen of hypodermic needles instead of ordinary steel needles, which nowadays are difficult to get of sufficient fineness.

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H. D.

## DISEASES OF THE SPLEEN

In the first number of a new journal, *Anales de Parasitología y Hematología,* published in Madrid, Asua deals at length with diseases of the spleen.

The spleen has physiological, defensive, and compensatory reactions. The physiological reactions include (*a*) formation of lymphocytes and large mononuclears, (*b*) destruction of red and white cells, and (*c*) inhibitory effect on bone-marrow function, shown by the appearance of Howell-Jolly forms in the blood if the spleen be removed, and by a diminution in the resistance to salt solutions of red cells subjected to the influence of the spleen. There are further excitor effects on nitrogen, carbohydrate, and fat metabolism, and less evident effects on digestion.

Defensive reactions are the formation of macrophages, myeloid metaplasia leading to increased output of polymorph phagocytes and also formation of bactericidal substances. Sarcomatous metaplasia is included as a defensive reaction, and also the myeloid metaplasia seen in some anaemias.

The true compensatory function is that evidenced by splenomegaly in various endocrine defects.

Asua then passes on to a classification of blood diseases designed to bring out the position of those in which the spleen is most affected. In his first group of anaemias, primary haemopathic anaemias, that due to loss of blood stands alone. The second group corresponds to the myelophthisic anaemias of some authors and is styled the group of primary myelopathic anaemias. It contains the anaemias of multiple myeloma, leukaemia, &c. The third group, haemomyelotoxic anaemias, includes most of the commoner varieties. There are first those of exogenous causation, e. g. following administration of blood poisons or the toxins of acute infective disorders. Secondly are the endogenous, including anaemias which are merely a part of the general debility attending chronic disorders either neoplastic or infective, and thirdly, a group of endocrine disorders. Dependent on splenic disorder, which is thus elevated to a position of primary aetiological importance, we have Banti's disease and haemolytic icterus, while chlorosis is included as depending on ovarian abnormality. Pernicious anaemia fills the third group of haemomyelotoxic anaemias, those of complex causation.

The polycythaemias are also classified, first, into the compensatory and the pathological. Compensatory polyglobuly includes the spurious form seen in emphysema, and the true (as depending on blood destruction) as seen in some cases of poisoning by haemolytic drugs. Pathological polyglobuly is seen in Vaquez's disease and in some cases of tuberculosis, after splenectomy, &c.

The remainder of this long paper is devoted by Asua to consideration of the clinical aspect of diseases of the spleen. He considers that Banti's disease and haemolytic icterus are joined by a series of intermediate cases, and groups them together as hypersplenic disorders. The contrary group, asplenia, does not correspond to any recognized clinical entity, but two cases are given of which one may have been hydatid of the spleen. Defect of spleen function might, of course, be recognized by the absence of signs of its physiological functions already detailed, and it is evident that the removal of inhibitory influences of the bone-marrow leading to polycythaemia bulks largely in Asua's mind.

This paper is somewhat restricted in scope, and includes no notice of leukaemia, Gaucher splenomegaly, or other diseases of this group, but Asua has certainly collected a vast amount of information with regard to the infective and endocrine disorders as affecting spleen function, and this is fully and lucidly set forth.

**Splenic anaemia.** Mayo propounds the thesis that splenic anaemia is a clinical entity, i. e. a syndrome which occurs when the spleen is fibrosed, no matter what the original cause of the fibrosis may have been. He considers that the spleen destroys an increased number of red cells when it is fibrotic, and that the marrow fails to make up the loss. A chronic anaemia results, which can be remedied by removal of the spleen.

Aschenheim considers that splenic anaemia of infancy, the von Jaksch syndrome, is a definite morbid entity due to an inherent weakness of the haemopoietic organs. He admits that rickets has a great share in the disease, but would appear to hold that it could not produce it if the inborn weakness were not present.

**Abscess of the spleen.** Cutler reports a case of abscess of the spleen following otitis media, and gives references to the literature. The case is of interest, amongst other reasons, because there was very slight leucocytosis until the abscess burst, when the resulting peritonitis caused a large increase. This accords with the views of Audain on the significance of leucocytosis.

**Gaucher's disease.** Sappington reports a case of Gaucher's disease in a man of 50 who died from gunshot wounds administered by the police. There was no history of ill-health, but very little could be ascertained about the patient's antecedents. At autopsy it was noticed that the liver 'exhibited what looked like a moderate chronic hepatitis', and the retroperitoneal glands were moderately enlarged. The spleen 'was in general soft . . . but scattered all through it were firm nodules more apparent to the palpating finger than to the eye . . . on section, the firmer areas were not plainly discernible . . . the general colour was normal'. The spleen was submitted to Mandlebaum for examination, who pronounced it typical of

Gaucher's disease. Sappington throws out the suggestion that the disease is perhaps more frequent in Jews. Chemical investigation did not reveal the presence of lipoids.

In an important paper Mandlebaum and Downey conclude that none of those pathological or experimental conditions which present a superficial resemblance to Gaucher's disease are really identical or even closely analogous.

Their observations show that the 'glassy' cells characteristic of Gaucher splenomegaly are derived from the reticulum, although a possible origin from endothelium as well is not quite disproved. These cells never contain anisotropic bodies, myelin substances, or neutral fats, as may occur in diabetes with lipoidaemia, &c. Moreover, these cells are by no means of the definite oval type usually insisted on. They are to be regarded as reticular cells suffering a particular 'glassy' change, and vary in shape and attachments from the normal reticular cell in which changes are just beginning to the free oval or circular cell, whose uses in bodily economy are probably at an end.

Mandlebaum and Downey believe that the disease is caused by some metabolic disturbance, but hazard no suggestion as to what caused the metabolic disturbance which caused the disease. They give a full bibliography.

**Sarcoma of the spleen.** According to Duchemin, who records a fatal case, primary sarcoma of the spleen is very rare. Only about 24 cases have been published, of which 11 were not discovered until the autopsy. Of 13 treated by splenectomy 4 died as the result of the operation, and of the 9 survivors 4 died of a recurrence, 1 was lost sight of, and 4 made a good recovery. In Duchemin's case the disease had a rapid course without characteristic symptoms, being manifested first by moderate enlargement of the spleen and anaemia, and then by cachexia. A diagnosis of malarial spleen was made owing to the definite action of quinine. But the improvement produced was mainly local and not general, whereas in malaria just the opposite occurs. Duchemin suggests that this discordance in the clinical symptoms may facilitate the diagnosis between a malarial spleen and a malignant growth.

**Tuberculosis of the spleen.** According to Giffin (1), who records an illustrative case in a girl aged 16, so-called primary tuberculosis of the spleen is not exceedingly rare. It is impossible to say that it is ever strictly primary, for it is almost always certain that an original focus was formerly present elsewhere in the body, though no evidence of tuberculosis may be found at the time of examination. The disease may produce an anaemia of the haemolytic type, and splenectomy, as in Giffin's case, may result in complete cure. Secondary tuberculosis of the spleen, which is quite common, is usually miliary in type and very rarely caseous. Giffin is of opinion that from the standpoint of diagnosis tuberculous splenitis should be considered in every case with marked splenomegaly, in which the findings are not clearly those of some other disease.

**The spleen in abdominal cancer.** According to Richard, who devotes his Lyons thesis to the subject, the size of the spleen in abdominal cancer does not appear to have attracted much attention. From a study of the literature he comes to the following conclusions: (1) In cancer of the stomach the spleen is atrophied. The exceptional cases in which its size is increased are due to secondary infection in the ulcerated neoplasm, concomitant disease or involvement of the spleen by the cancer. (2) The spleen is atrophied in massive cancer of the liver, enlarged in adeno-carcinoma with cirrhosis, and not affected in secondary carcinoma of the liver. (3) There is no general rule as regards the size of the spleen in cancer of the extrahepatic bile-ducts, or in cancer of the pancreas, but the spleen is usually enlarged in cancer of the head of the pancreas and diminished in size in cancer of the body and tail of that organ. (4) Cancer of the large intestine, especially of the sigmoid flexure, is accompanied by atrophy of the spleen. (5) The spleen is enlarged in new growths of the kidney, but atrophied in those of the uterus. (6) Secondary cancerous growths in the spleen may occur, but are rare, Richard having found only seven examples among 214 cases of abdominal cancer.

**Various forms of splenomegaly.** In an article published on March 31, 1919 entitled 'War Splenomegaly?' Luccarelli states that for more than a year he has met with enlargement of the spleen in a considerable number of soldiers without being able to connect it with any present or past disease such as malaria, enteric fever, spirochaetosis haemorrhagica, or trench fever. The following explanations are suggested: (1) a toxic state of intestinal origin due to the food and the character of the life at the front, including nervous impressions, emotions, fear, &c.; (2) an abortive form of trench fever; (3) the presence of the *Spirochaeta ictero-haemorrhagiae* or other unknown organisms or causes.

In an article on the Wassermann reaction and chronic splenomegaly, Weil records 12 cases of chronic splenomegaly, in seven of which a positive Wassermann reaction was obtained, although there was no evidence of syphilis, inherited or acquired. Antisyphilitic treatment had no effect on the splenomegaly or the Wassermann reaction, but caused an aggravation of the general condition. The positive reaction could not be regarded as due to the splenic lesions, as in three of the five negative cases leukaemia was present. Weil suggests that the positive reaction was due to some unknown parasite.

Bradford describes an obscure and rare disease of which he had seen only about three examples. It was characterized by a febrile illness closely resembling enteric fever and lasting several weeks, during which the spleen slowly increased in size to that reached in ordinary splenomedullary leukaemia, from which the cases differed in that after an illness of several weeks the pyrexia declined and the spleen slowly returned to normal. The blood-examination showed a condition similar to that of splenic anaemia, a diminution of the red cells and a considerable leucopenia. Repeated examination of the blood and stools failed to reveal any organisms of the enteric group, and the Widal reaction was uniformly negative.

Tuohy reports an unusual case and is unable to find anything similar in the literature. The salient features were leucocytosis and splenomegaly. The leucocytes reached as high as 65,000 before splenectomy and 240,000 afterwards. The patient was a woman of 40 and complained when first seen of acute symptoms referable to perisplenitis. So far there is little in the case to differentiate it from leukaemia, but the differential count was remarkable in that there were 99 per cent. of polymorphonuclear leucocytes. No mention is made of any myelocytes or abnormal cells of the white series, but there was a mild degree of anaemia with a few nucleated red cells. The patient was lost sight of, but reports showed that her health improved after operation. Four months later she was re-admitted with influenzal pneumonia and died before any investigation could be made.

In a paper entitled 'Persistent eosinophilia with hyperleucocytosis and splenomegaly', Giffin (2) describes a case which seems to be unique in medical literature. It therefore requires detailed notice. A man, aged 31, presented himself for examination in the year 1913. Then, and at various later dates, he suffered from symptoms referable to obliterative pericarditis, e. g. oedema of legs and signs of heart failure, and these should probably be traced to a prolonged fever terminating in pneumonia from which he suffered eight years previously. At the same time he suffered from a series of symptoms similar clinically to those of some cases of Hodgkin's disease, viz. general enlargement of glands, splenomegaly, pruritus, and eosinophilia. A lymph gland removed from the axilla showed 'a moderate inflammatory reaction. The germ centres were intact; a marked endothelial hyperplasia was present. Eosinophil polynuclears were quite numerous and a few scattered eosinophilic myelocytes were to be found.' For a full year the patient remained in very fair condition with the exception of mild anaemia of the chlorotic type and persistent eosinophil leucocytosis. Repeated search for all sorts of parasites was negative and it was decided to perform splenectomy. This was done and the patient benefited considerably, but the glandular enlargement persisted and the leucocytosis became enormous, on one occasion 208,000 with 83 per cent. of eosinophils.

Two years after splenectomy pruritus developed and was thenceforth a source of trouble, and six years after coming under observation he died of pneumonia.

The spleen at operation showed Malpighian bodies intact but not numerous, marked cellular hyperplasia and slight increase in fibrous tissue. Eosinophils were very numerous but eosinophil myelocytes very few. The bone-marrow at autopsy was hyperplastic and contained great numbers of eosinophil leucocytes. The erythrogenic function seemed to be almost completely in abeyance. The liver showed 'cirrhosis of a mild grade', but no further details are given. There were also present fibrous pleuritis and pericarditis and perihepatitis. There had been very marked perisplenitis at operation.

Giffin states that Stillman reported a similar case in 1912 and refers to one or two cases of Hodgkin's disease which were in various ways analogous to his own. He was unable to suggest any diagnosis, but considers that the splenectomy was responsible for the high figure reached by the white cell count.

Lévy-Franckel records two cases of splenomegaly following injection of neosalvarsan. The patients were a boy aged 13 with lupus, and a soldier with psoriasis, in both of whom the Wassermann reaction was negative and there was no evidence of syphilis. Leukaemia and pseudo-leukaemia could be excluded by examination of the blood, and the subsidence of the splenomegaly after cessation of the treatment negatived the diagnosis of primary tuberculosis or cancer of the spleen. Lévy-Franckel therefore concludes that the splenomegaly was due to the neosalvarsan, although no previous cases of splenomegaly due to this cause have been recorded.

After preliminary remarks on the difficulties in diagnosis presented by all cases of splenomegaly, Beckmann points out that in no disease are these more evident than in haemolytic icterus.

He considers the increased fragility of the erythrocytes as an all-important diagnostic point, and it occurred to him that where the diagnosis was still in doubt owing to the absence of increased fragility, this sign might be produced by provocative methods similar to those used in malaria.

He therefore exposed two patients to the direct rays of the sun, gave alternate hot and cold douches and massage over the spleen, and finally a dose of X-rays. By these means in two cases he reduced the resistance of the red cells so that whereas they had formerly resisted haemolysis until a dilution of 0·34 per cent. saline was reached, they now suffered complete haemolysis in 0·38 per cent. The diagnosis was thus established.

In two other cases already exhibiting fragility there was no change under the same provocation. He considers that the fragility of the red cells is due to substances in the circulation and not to inherent marrow defect, and discusses at some length published views on this point.

The patient seen by Losio had been under medical care on several occasions, and the question of malaria was raised at an early date, but no confirmatory evidence was found. He had been treated by X-rays and iron and arsenic—each time with but temporary benefit. The Wassermann reaction was negative, as was the family history. Clinically the diagnosis of haemolytic icterus was fully established.

Very free venous anastomosis rendered the operation one of no small difficulty. Microscopically the spleen showed no very marked changes beyond congestion and thickening of the trabeculae. Pigment in any form was but slightly in evidence. The arteries, however, were much thickened, the intima being particularly affected. The patient made a good recovery, but the fragility of the red cells had not returned to normal when the blood was last examined.

The family studied by Biffis consisted of four generations; in the first, three, in the second, four, and in the third, three were sufferers from haemolytic splenomegaly of the common familial type. In the fifth generation were five children, descended from three of the previous generation, but inheriting the abnormalities of their parents in a partial but recognizable degree. Of these five children there was not in every case opportunity for a complete examination. The details elicited were as follows:

Palmira, aged 7. Debilitated, headache; pain in the left side of the abdomen; fever; gastric disorder; diarrhoea; numerous small glands; no icterus of the conjunctivae; lungs normal; apical systolic bruit; liver and spleen not palpable; blood examination refused.

Germana, aged 15, sister of above. No icterus; numerous glands; infantile appearance; spleen enlarged; liver not enlarged; thorax normal; blood examination refused.

Emilio, aged 15, student. Good general condition, but pallor evident; numerous small glands; spleen palpable and hard; no anaemia, but 3–5 per cent. of reticulated reds and slight anisocytosis; resistance normal; serum contained urobilin and agglutinated the red cells of his sister.

Anastasia, aged 12, sister of the above. Pallor; epistaxis; icterus of conjunctivae; several small glands; apical systolic bruit; lungs normal; spleen felt to be hard and painless on deep inspiration; haemoglobin 60 per cent.; 4–5 per cent. reticular cells; fragility normal; auto-agglutination of her own red cells present and of those of her brother and of her uncle.

Alessandro, aged 13. Indigestion; pain in left hypochondrium; diarrhoea; pallor; many small glands; liver enlarged; spleen not enlarged; trace of icterus; haemoglobin 8 per cent.; 3 per cent. of reticular cells; no urobilin or bilirubin in serum.

Biffis enters fully into the theoretical considerations to which these cases give rise.

Keisman records a case of splenogenous thrombopenia in a girl aged 17, who for several years had suffered from increasing enlargement of the spleen with marked retardation of physical development. Signs of a haemorrhagic diathesis soon appeared, the first evidence of which was severe epistaxis, which was followed by haemoptysis and bleeding from the gums. Rapid recovery followed removal of the spleen. The blood picture before operation was that of secondary anaemia associated with the haemorrhagic diathesis and thrombopenia. After splenectomy a definite leucocytosis up to 14,000 appeared, and the number of blood-platelets within 6 hours of the operation increased from 45,000 to 224,000. Not only did the haemorrhages disappear, but an increase in weight and general development took place, and menstruation which had hitherto been in abeyance appeared.

**Splenectomy.** According to Kleeblatt, splenectomy is indicated in isolated miliary tuberculosis of the spleen, in all processes associated with increased haemolysis, such as haemolytic jaundice, hypertrophic cirrhosis of the liver, the first and second stages of Banti's disease, and, as a last resort, in the third stage. In pernicious anaemia the operation has a temporary success. Splenectomy is contra-indicated in portal thrombosis and in all processes caused by primary portal congestion and in polycythaemia.

Bellingham Smith reports the case of a boy who had undergone splenectomy five years previously and was in good health. The symptoms at the time of operation had been splenomegaly, leucopenia, and general debility. The Wassermann test was positive, and the liver was seen to be cirrhotic at operation. As antisyphilitic treatment had been quite useless, the excellent result from splenectomy is the more noteworthy. Bellingham Smith also mentions a case of acholuric jaundice in which the operation was fatal from the supervention of pneumonia.

McConnell is to be congratulated on reporting a fatal case of splenectomy for cirrhosis of the liver, i.e. a failure and one of those cases which is so often more instructive than a success. The considerations which led to operation are discussed fully and are eloquent of the ever widening sphere of the operation of splenectomy.

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## BILIARY SURGERY

The number of communications on biliary surgery which continue to appear show the extent to which operative treatment has developed. Nevertheless there are no generally accepted criteria between the cases suitable for medical treatment by purgation and those in which operative treatment is indicated. It is probable that in the majority of cases of biliary disease medical treatment is continued until chronic jaundice, sepsis and malignant disease produce complications too far advanced for successful surgical interference. The drainage of the gall-bladder has proved unsatisfactory, is generally condemned, and avoided whenever possible. Excision of the gall-bladder has become the most frequent operation. When performed on early cases, there may be said to be no danger of death. C. H. Mayo reported 2,460 cholecystectomies following cholecystitis in the course of three years with a mortality of 1·8 per cent.; Maccarty reported the examination, between 1913–1919, of 4,998 gall-bladders removed at the Mayo Clinic, the pathological changes described being of a relatively early kind. Against this must be set the experience of city hospitals, admitting cases suffering from acute complications involving the pancreas, liver, peritoneum, heart, &c. An unsatisfactory feature of these early cholecystectomies is that in a certain proportion there is a relapse after some months, when it may be found necessary to establish an anastomosis. Then the premature excision of the gall-bladder may be a matter of regret.

It is continually repeated that an analogy between the appendix vermiformis and the gall-bladder affords a justification for the excision of the latter. It is needless to point out the differences between the two. Patients over fifty who have long been under medical treatment for chronic jaundice, however slight and intermittent, are likely to die after operation owing to recurrent capillary haemorrhage and degeneration of the myocardium. Septic complications spread both to the peritoneum and to the hepatic veins. The longer the biliary disease has lasted the more likely is it that the pancreas is involved. Also after 40 years in 5 per cent. or more of long-standing cases malignant disease supervenes, and in only a very few has it been possible to remove the new growth.

**Anatomy and physiology.** The gall-bladder, by its glands, forms mucus to mix with the bile; its muscular coat and nerve-supply furnish the mechanism for its rhythmic contractions, the flow in the ducts being aided to a certain extent by inspiration. The function of the gall-bladder may therefore be described as of no great importance, and in the majority of cases it can be dispensed with. This still leaves open the question whether in a minority of cases there is full compensation for its loss.

An important anatomical point is the junction between the hepatic and cystic ducts to form the common bile-duct. Whilst the length of the pancreatic and retroduodenal segments of the common bile-duct are anatomically constant there is variation as to its origin and in the length of the supraduodenal segment. Pallin has traced these variations to the end of the second or commencement of the third month of foetal life. The typical junction is constituted by the secondary hepatic ducts joining into one hepatic duct which is about 2·5 cm. in length. This unites with the cystic duct at an acute angle. But the hepatic duct may be prolonged and the cystic duct run parallel with it before uniting, so that there may be hardly any supraduodenal segment of the common bile-duct. The hepatic duct may then have a length of 5 cm. The cystic duct may not run parallel but have a spiral course so that its junction with the hepatic duct is in front.

The cystic artery arising from the hepatic passes behind the hepatic duct to approach the cystic duct from above and behind.

The ligature of the cystic duct at its termination without infringing on the common duct and without leaving a segment of the cystic duct behind as a blind pouch, also the separate ligature of the cystic artery to prevent recurrent haemorrhage, cannot be carried out with certainty when excising the gall-bladder, unless this junction of the ducts is first exposed to view, e.g. by the method recommended by Behrend, noted below.

Those animals which have no gall-bladder have developed in the wall of the common bile-duct muscular tissue, also elastic fibres which enables the duct to dilate and contract, whilst the discharge of bile is regulated by the sphincter at the papilla. Hence, in order to compensate in man for the loss of the gall-bladder, the common bile-duct must be able to act as in animals, and the function of the sphincter papillae must be unimpaired.

**Pathology.** Gall-stones are so often found in the gall-bladder in the course of post-mortem examinations that their presence is, by many physicians, still held to be of hardly any importance. On the other hand, it is widely held that, however slight, gall-stones always show their presence. If all cases, however vague the symptoms, were submitted to X-ray examination, it might be possible to demonstrate the presence of calculi otherwise undiscoverable.

It is difficult, before the operation, to say whether the biliary trouble has arisen by infection through (*a*) the hepatic artery; (*b*) the portal vein; (*c*) through the duodenum and common bile-duct; (*d*) through the lymphatics, or (*e*) by direct contiguity. In particular, as regards typhoid fever, typhoid bacilli are said to be always present in the bile of the gall-bladder, but cholecystitis as a complication of typhoid fever is quite exceptional. During the war paratyphoid was occasionally complicated by cholecystitis, but this did not require operative treatment.

In Deaver's case acute infective cholecystitis occurred in a girl, aged 5, after typhoid fever, but she was already convalescent. No typhoid bacilli were found in the pus mixed with blood contained in the gall-bladder, nor was the typhoid reaction obtained from the bile. The bladder was incised and drained, the resulting fistula requiring later to be closed by operation.

Gall-stones are supposed, in the absence of inflammation, to be formed by concentration and stagnation of bile, leading to the deposit of cholesterin in laminae. Hesse, basing his statements on the observation of 17,402 post-mortems in St. Petersburg, found gall-stones in 0·73 per cent. of men and 4·75 per cent. of women, gall-stones being comparatively rare in Russia. Others have found gall-stones in as many as 10 per cent. In 84 per cent. of the cases Hesse said there had been no previous signs, the majority being found between the ages of 50 and 60.

X-rays are being employed with increasing efficiency for the detection of gall-stones; when lime has been deposited there is a relative opacity; when the stone consists of pure cholesterin, there is a translucency in comparison with the shadow of normal bile, suggesting air bubbles. But so far these have been merely confirmatory observations; the absence of such in no way contra-indicates an exploration. As the cause or causes of concentration of the bile are obscure, the source of gall-stones remains unexplained, when no inflammation has preceded their formation. When animals are infected by micro-organisms experimentally, the organisms with which the animal has been inoculated are to be found in the bile of the gall-bladder. Inflammation once set up, it is easy to explain the formation of gall-stones from epithelial débris containing cholesterin and the lime salts of the bile-pigments. But then cholecystitis does not necessarily lead to the formation of gall-stones.

Once formed, there appears to be no evidence at all that gall-stones are diminished in size or dissolved in any way.

**Biliary obstruction not due to gall-stones.** The congenital obliteration of the bile-ducts affects the extrahepatic portion. In a case described by Dickson the child at birth appeared healthy; there was rapidly increasing jaundice from the second day followed by coma and death within three days of birth. The intrahepatic bile-ducts were dilated by bile, and there was a little recent small-celled infiltration and cloudiness of the hepatic cells, which were packed with pigment, but no biliary cirrhosis. The cystic, right and left extrahepatic, and the common bile-ducts were impervious cords. The only other lesion was congestion of the suprarenals with haemorrhages.

Holmes, in reviewing more than 100 recorded cases, reached the same conclusion that the obliteration occurred outside the liver. In more than 16 per cent. the common duct only was found obstructed, the cystic and hepatic ducts being well formed. When such is the case the conditions are the more favourable for the success of an anastomosis. The particular case he described died at the age of 15 weeks. All the tissues were markedly bile-stained; the liver, a deep purple, showed biliary cirrhosis; the intrahepatic ducts normal, and not dilated; the gall-bladder a fibrous cord with two dilatations containing greenish-black mucus. Three extrahepatic ducts met in a common diverticulum 2–3 mm. in diameter at the junction of the cystic and hepatic ducts. A fibrous cord without a lumen replaced the common duct down to the papilla. The pancreatic ducts were normal. Here also the diverticulum at the junction offered an opportunity for an anastomosis.

**Cyst of the common bile-duct.** When the common duct undergoes a stenosis near its termination, it may become dilated into a cyst. Connell collected 36 cases in which a cyst had formed as a diverticulum up to the size of a man's head. It extends behind the peritoneum towards the right kidney whilst pushing the duodenum forward, and to the left and the transverse colon downward and to the left. The diverticulum takes origin in the upper and middle third of the common duct, the hepatic, cystic and commencement of the common duct being normal. There is present a cystic tumour with symptoms of biliary obstruction for which an anastomosis with the duodenum or jejunum should be done; both drainage and extirpation being wrong.

**Kinking of the cystic duct** may be recognized as following the drainage of the gall-bladder. The fundus being fixed to the abdominal wall, the gall-bladder shrinks and drags on the cystic duct, which in its turn may give rise to a kink at the junction with the hepatic duct. In such a case the discharge consists of mucus, whilst the symptoms of biliary obstruction persist in spite of the drainage of the gall-bladder. Schmeiden also explained some cases as due to a kinking of the cystic duct owing to the gall-bladder becoming over-distended. The cases exhibited symptoms of a slow intermittent retention in the gall-bladder attended by some pain but without jaundice, fever, or severe attacks of colic. The attacks of pain, are of short duration, they occur when an over-filled gall-bladder contracts upon a kinked cystic duct. Between the attacks, all symptoms may be absent. It is impossible to distinguish a kinking from obstruction by a calculus until an exploration is undertaken. The treatment should be that of cholecystectomy.

**Early cholecystitis.** Maccarty's description of the early histological changes resulting from cholecystitis was drawn from the examination of 4,998 gall-bladders removed, in 96·5 per. cent. of which there were gross pathological lesions as follows: congestion and oedema of the villi: local and general lymphocytic infiltration of the mucous membrane: in the villi fibrotic changes. In the mucous membrane and submucous tissue large spheroidal cells collect filled with a fatty material, and it is this which gives the so-called strawberry-like appearance to the interior of the gall-bladder. If papillated, the papillae have a yellow or whitish look.

**Reflex gastrospasm.** Lüain described a local spasmodic contraction of the stomach occurring with cholelithiasis, as noted by observing the passage of a bismuth emulsion under the X-rays. Total gastrospasm is rarely observed; an ulcer on the lesser curvature leading to the formation of an hour-glass contraction gives rise to a circular spasmodic contraction. A spasmodic contraction affecting the pyloric end of the stomach may be noted as of regular occurrence when there is cholelithiasis. The stomach otherwise appears normal under the X-rays, but as the emulsion passes, the pyloric region may show a narrow wavy channel, lighter than the rest of the stomach, following which some of the emulsion is found to have reached the duodenum.

**Operative procedures. Incisions.** The incisions employed for exposing the region of the gall-bladder vary—some commence, at any rate, with a vertical incision through the middle line or right rectus. Transverse incisions are warmly advocated because running parallel to the course of the nerves to the recti muscles. If the recti are cut across it is essential that afterwards sutures should be passed so as to unite the sheath both underneath and superficial to the muscle, in order to prevent hernia. When there is a great depth of subcutaneous fat, the superficial incision used by Seelig offers a better opportunity for retraction. Commencing over the xiphoid cartilage and ending a little to the right of the middle line about the level of the umbilicus, an incision convex to the right includes skin, subcutaneous tissue and the external oblique aponeurosis together with the anterior sheath of the rectus. The semicircular flap being raised the deep incision can be made vertically or transversely.

**Cholecystectomy.** It was recommended long ago, both by the Mayo brothers and by Moynihan, that in performing cholecystectomy a commencement should be made by exposing and dividing the cystic duct, at the same time that the cystic artery is ligatured. To do this Behrend drew up the liver and gall-bladder to the right, and the pyloric end of the stomach over to the left. The edge of the gastro-hepatic omentum is thus rendered tense, its free border is then incised. The junction of the hepatic and cystic ducts to form the common duct, the portal vein, the hepatic artery and its cystic branch can then be identified. Unfortunately a great number of cases have advanced too far for such a procedure. The structures are obscured by enlargement of lymphatic glands along the cystic, hepatic and common bile-ducts, which also become buried in oedematous fibrous tissue. All that can then be done is to commence separating the fundus of the gall-bladder until a pedicle is reached, including the cystic duct and artery, which are ligatured by transfixion. Care must be taken to leave behind some of the cystic duct rather than to encroach upon its junction with the common duct.

**Cancer of the bile-duct.** Malignant disease involving the biliary tract has been unsuccessfully treated hitherto. Pallin first gave an account of 52 cases of malignant disease involving the bile-ducts which had been published in Sweden, including the surgical treatment of some of the cases. The cases complicated by cancer were about 1–2 per cent. of all cases in which gall-stones were found. Kehr's German experience was the same, 31 cases of cancer among 2–3,000 cases of biliary disease. Cancer attacks the bile-ducts between the ages of 40–70, especially in women, one-third of the cases arise at the papilla. Cancer of the common duct, at the junction of the cystic and hepatic ducts, or of the hepatic ducts, is more common in men. The frequency at the papilla of Vater is explained by the impossibility of drawing a sharp line as to the starting-point of the cancer, whether at the termination of the bile-duct or in the mucous membrane of the pancreatic duct, or of the duodenum. A particular characteristic of carcinoma at the bile papilla, is a papillated growth projecting like the end of a finger into the lumen of the duodenum. The other forms of early cancer of the bile-duct is a tumour the size of a hazel-nut or walnut, a diffuse scirrhous infiltration constricting the lumen, or a tubular formation, especially attacking the hepatic ducts. The microscopic structure is essentially the same, consisting of cylindrical epithelium separated by various amounts of malignant fibrous formation. Pallin differs from the accepted view that cancer originates by the irritation set up by gall-stones. Of the 52 cases, gall-stones were found only in 13, chiefly in the women and in those over 60 years of age. The finding of a stone in the middle of a cancer does not appear to him to be evidence of the causation of the cancer by the stone—jaundice is the clue. Symptoms and death are usually due to the cholaemia rather than to an extension of the growth. Attacks of fever and pain are exceptional, and then only when the cancer is at the papilla as a late complication. The distension, or absence of distension, of the gall-bladder is a sign of a very dubious character, and even if distended it may not be palpable. When the cancer involves the hepatic ducts, the gall-bladder should be small; when at the junction of the cystic, hepatic and common ducts, it may be distended with mucus; when involving the common duct and papilla the gall-bladder may be distended with bile, yet not palpable. If the growth spreads to involve the gall-bladder it may shrink. A variable jaundice with a palpable swelling may be due to chronic pancreatitis. Catarrhal jaundice should subside within a month and there should be no enlargement of the gall-bladder. It is more easy to exclude cancer at ages below 40.

As to the palliative treatment, drainage is always bad owing to the loss of bile. Anastomosis is especially indicated, and the relief given depends on the stage of the disease, but an anastomosis connecting the hepatic ducts is very difficult to carry out. Among the Swedish cases were 9 anastomoses, of whom 3 survived the operation, 2 cholecyst-jejunostomies, and a cholecyst-duodenostomy. They survived about 6 months each, 2 being relatively relieved, and one not freed from jaundice and in bed all the while.

Four cases were submitted to excision, 3 of cancer at the papilla, all of whom died of the operation. One case survived after excision of cancer at the junction of the ducts followed by a hepatico-duodenostomy. There was relief for 10 months; death occurred 11 months after the excision, when metastatic growths were found in the liver, but there was no recurrence *in situ*. Of 44 cases collected from the literature 23 recovered from the operation. Of these, one of Körte's cases, an excision of a cancer at the papilla of Vater exposed through the duodenum, followed by drainage of the hepatic duct, was free from recurrence 6 years after the operation. Navarro's similar case was alive without recurrence more than two years after the operation. Of the remaining 21, 14 were known to have died of recurrence, 6 *in situ*, and 5 of metastatic disease, 2 cases survived the operation 2½ years.

The indications, therefore, are for excision if practicable, generally for anastomosis; failing either of these, the exploratory wound should be closed without drainage.

**Anastomosis.** There does not seem to be much difference between an anastomosis with the duodenum, jejunum or stomach. It should depend upon which procedure is the more practicable, care being taken that the gall-bladder is not drawn upon so as to kink the cystic duct. Mathieu recommended the anastomosis with the stomach because there would be lees chance of ascending infection. He had operated on three cases for symptoms of biliary obstruction, and being unable to find the cause, decided that the excision of the gall-bladder was not indicated. The three cases had been relieved of all trouble up to date. Dujarier had done this twice, in one biliary obstruction recurred after some months. In the discussion on the above cases Tuffier and Quénu suggested that such obscure cases of biliary obstruction often turned out to be pancreatic in origin.

To unite the hepatic duct to the duodenum C. H. Mayo recommended that adhesions should be disturbed as little as possible when defining the open end of the hepatic duct. A triangular flap of peritoneum should be turned down from the duodenum (or from the prepyloric part of the stomach). Then a short length of a rubber catheter is taken, and a small collar made from india-rubber tubing of a size next above that of the catheter is slipped over each end, and one end is inserted into the hepatic duct, the other through a slit in the duodenum. Then the peritoneal flap is sewn down and thus the tube is kept in position for a time by the collars.

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## CONGENITAL TORTICOLLIS

The pathology of Congenital Torticollis, its causation, the nature of the changes in the sternomastoid muscles, and the indications for treatment, continue the subject of controversy. Meanwhile, the cases mostly come under the surgeon long after infancy, so that then the removal of the contracture of the sternomastoid muscle fails to abolish established secondary deformities, asymmetry of the face, lateral curvature of the spine.

One of the common statements on the subject is that the muscle is ruptured during birth, especially when a breech presentation entails traction on the aftercoming head. Another attributes the condition to intra-uterine disease, in particular to inherited syphilis. Nerve paralysis, and ischaemic rigidity produced by the partial cutting off of the blood-supply, have been proposed as causes.

Sippel has contributed observations on 13 infants born with wry-neck. He supplies in his cases evidence as to the position of the infant in the uterus, in order to show that the changes in the sternomastoid muscle are the result of the head of the foetus being turned to one side, so that the point of the shoulder of that side is pressed into the neck. This produces an atrophy and contracture of the muscle, affecting especially its deeper part, also an atrophy of the overlying platysma. Forcible straightening of the head during birth causes haemorrhage into an already atrophied, partially fibrosed and contractured muscle, when the subsequent changes in the muscle are a combination of the pressure atrophy and of the haemorrhage. But if there is no strain upon the muscle during birth, the torticollis is solely attributable to the abnormal pressure upon the muscle towards the end of intra-uterine life.

An infant born with wry-neck requires active treatment forthwith. In slighter cases massage and movement of the head, so as to stretch the shortened muscle suffice. In more marked cases the fibrosed and contractured portion of the muscle should be excised as soon as the child is about a month old. The cause of the wry-neck is thus removed and there is left a fine extensile band. The head is held straight and can be turned freely to the opposite side; the temporary flattening of the skull and asymmetry of the face disappear. In none of the cases referred to below did the child show any lateral curvature of the spine; early cure of the wry-neck prevents its occurrence subsequently.

A skiagram of a foetus, late in a normal pregnancy, shows it with the head fully extended on the spine, looking straight forward. It is no longer to be taught that the head is kept flexed with the chin against the sternum. In consequence of a scarcity of the amniotic fluid, of a narrow pelvis, of a contraction of the uterus above the cervix, of a twin pregnancy, the head ceases to be suspended and to move freely in the fluid. It is held fixed, turned to one side, with the shoulder pressing into the neck of that side. The arm of the same side, in particular the elbow, is so fixed as to hold up the head of the humerus. There is thus produced atrophy by pressure of the sternomastoid muscle and the overlying platysma sometime after the 5th or 6th month of pregnancy. This cramping of the foetus favours a breech or transverse presentation, but as shown in the skiagram given by Sippel, one side of the head may be forced down into the pelvis with a bending of the neck to one side, if the scanty amount of fluid allows the wall of the uterus to press unduly upon the buttocks above the pelvis; at the same time the spine becomes acutely flexed.

*Case I.* A primipara aged 28 had been admitted for haemorrhage at the end of pregnancy. A skiagram showed the foetus in the left dorso-anterior transverse position with the head sharply bent to the left upon the neck, and the head of the left humerus occupying the concavity formed by the bending of the neck. A skiagram of a more regular transverse presentation, reproduced for comparison, shows the foetus as if lying on its back with its head on a pillow, directed straight forward.

The woman was delivered by caesarean section, when the position of the foetus was found to be as above noted. The amount of amniotic fluid was small. A small female child was seized by the feet and removed without any strain on its neck.

Otherwise normal, the child showed a marked wry-neck on the left side; the face on the left side was flattened, it squinted with the left eye, the skull over the region of the temporal bone of that side was depressed, the auricle was flattened and its lobule pushed up. The chin and mouth were turned over to the right. The left shoulder had been pressed into the neck below the ear and mastoid process, the arm had been elevated at the shoulder, and the forearm sharply flexed at the elbow. The left sternomastoid muscle was so shortened that when the head was turned straight, it was rendered tense, as seen in the photographs in the article. On being released, the head returned at once to the position characteristic of left torticollis. The muscle felt as if strongly contracted, and harder than its opposite. The right upper extremity had been freely extended by the side, with the shoulder low. A skiagram showed that there was no spinal curvature, but the left clavicle as compared with the right had an exaggerated S-shaped curve.

The infant was treated for three months by massage and turning of the head. Meanwhile the asymmetry of the face, the depression of the temporal bone and the deformation of the clavicle tended to disappear, but there was no stretching of the shortened muscle.

Therefore, at the end of three months, an incision was made over the left sternomastoid which was found shortened, pale, and atrophied. There was no marked fibrosis; the blood-vessels and surrounding structures showed nothing abnormal. A segment was removed from the muscle and the head fixed in a corrected position. A microscopic examination exhibited atrophy of the muscle, some of the fibres showing degeneration into a homogeneous substance with loss of both longitudinal and transverse striations. The degenerated fibres stained badly; the muscle fasciculi were small and thin, without any marked fibrosis. There had been no rupture of muscle, and there was no blood-pigment in evidence of any previous extravasation of blood.

*Case II.* A primipara aged 23 was admitted in labour after premature rupture of the membranes and the escape of a very little fluid. A skiagram showed the foetus presenting by the breech with the head bent sharply to the left upon the neck, and the left shoulder raised and pressed into the concavity of the neck. The child was born spontaneously up to the head, which was 'delivered easily without traction or pressure in a typical way following Veit-Smellie', and without any anaesthetic being required. The male child presented a characteristic left wry-neck with the same features as in the previous case, asymmetry of the face, depression of the skull, pushing up of the auricle, displacement of the chin to the opposite side. There was a deep hollow on the left side of the neck with the surface blue by extravasation of blood into the folds of skin and into the muscle underneath. The muscle appeared shortened and thinner than normal. The child died a few days later of pneumonia. The platysma on the left side was found very thin, the left sternomastoid muscle markedly atrophied and intimately adherent to the platysma, the blood-vessels were less developed than on the right side, there was no thrombosis in the thin walled veins. There was a recent extravasation of blood into the upper third of the muscle, which also extended between the superficial and middle layers of the deep cervical fascia; the deeper part of the muscle had the appearance of having been contused. The microscopic appearance of a transverse section of the upper third of the muscle in comparison with that of the right side showed fewer muscle bundles, the deeper layer of the muscle and the intramuscular septa were infiltrated by blood and the muscle fibrils largely destroyed.

*Case III.* A primipara aged 33 with a breech presentation, after several attempts, was finally delivered, the buttocks by the aid of hooks, the aftercoming head by forceps. A markedly asphyxiated female child presented a typical right-sided wry-neck, with suffusion of blood over the middle and upper third of the muscle, also the other conditions noted in the foregoing cases. It lived 24 hours. On examination the right sternomastoid appeared markedly atrophied as compared with the left, both its clavicular and sternal portions; it had been reduced to the size of a lead pencil; the platysma was also very thin. There was fresh blood in the upper and middle third of the muscle against which the right shoulder had been pressed, and the blood had been extravasated into the cervical fascia. The muscle was markedly shortened, felt dense, but presented no rupture. The left muscle was well developed, almost the thickness of a finger, of normal redness and consistency, without sign of venous congestion.

*Case IV.* A woman aged 22 was admitted in labour with her second child. The skiagram showed a left breech presentation with the head turned to the right and the point of the right shoulder pressed into the concavity of the neck. Very little fluid escaped; the female child was born spontaneously, except for the Veit-Smellie manipulation of the head, in which no force was used. There was a right-sided wry-neck together with the conditions previously noted. The child died a few days later of bronchopneumonia, when the right sternomastoid was found much shortened; at the junction of the middle and upper third in particular the muscle was dense, pale, atrophied, the platysma being also atrophied, whereas the muscle on the left side was well developed. A transverse section of the muscle showed changes affecting especially the deeper part; passing from the superficial aspect inwards, without any marked line of demarcation, normal muscle fibres had begun to be separated by an increased amount of fibrous tissue. In the centre and deeper part of the muscle there was the marked atrophy noted above; also there were signs of haemorrhage as shown by blood-pigment mixed with newly forming fibrous tissue, and recent infiltration of blood among atrophied muscle fibres.

*Case V.* A primipara aged 32 suffering from albuminuria and threatened with eclampsia exhibited a left head presentation, very little fluid had escaped. She was easily delivered by applying forceps to the head. The child, a male, showed a *right* wry-neck with the attendant changes. A second foetus was then found in a right dorso-posterior transverse position, very little fluid escaped on rupturing its membranes, it was easily delivered without question of strain on the neck because the aftercoming head was so small and the maternal soft parts already stretched. The second child, also a male, showed a *left* wry-neck, and it died 24 hours after birth. The platysma on the left side was atrophied and rendered tense by turning the head straight, the sternomastoid muscle being shortened and highly atrophied. The front part of the muscle as well as the deep cervical fascia in the anterior triangle of the neck was infiltrated by recent blood, the muscle where infiltrated appeared as if contused. The microscopic changes were those of atrophy with recent blood extravasation. The firstborn of the twins survived, and it was intended to operate upon it for wry-neck when strong enough.

*Case VI.* A woman aged 33, giving birth for the fifth time, was admitted in the seventh month for haemorrhage and rupture of membranes. After a tampon, two foetuses were born spontaneously, the first, a small male, showed no deformity and survived. The second, a large male, had a left wry-neck and bilateral talipes valgus. It repeated the conditions noted in Case I. After its death, 30 hours later, the left platysma was found extremely thin and atrophied; with the very atrophied and shortened sternomastoid it formed a tense band when the head was straightened. The pressure of the raised shoulder had been applied especially to the posterior part of the upper third of the muscle. The muscle under the microscope exhibited atrophy without haemorrhage.

The following cases came under observation some time after birth.

*Case VII.* A primipara aged 23 with a normal pelvis was delivered spontaneously, the left side of the head presenting; the child was a female, the amount of amniotic fluid which escaped was small. Three to four weeks after birth the mother noticed an increasing tendency to a left-sided wry-neck. When examined at the age of 7 months there was a marked left torticollis with asymmetry of the face. On straightening the head the muscle became tense, and on letting go the head at once returned to the abnormal position. The muscle felt thinner and more tense than on the opposite side, but not definitely hardened. After a month of massage and turning of the head without improvement, the muscle was exposed between the middle and lower third and a piece cut out. The separation of the cut ends left a hollow in the posterior triangle. The portion excised showed atrophy of muscle without sign of haemorrhage. Five months later the wry-neck had been completely removed, a depression persisting where the muscle had been divided.

*Case VIII.* A woman aged 31 with a normal pelvis had been delivered at term. A breech presentation had required only the Veit-Smellie method of delivering the head. The mother first noticed the right-sided wry-neck three weeks later, and the child, when examined at the age of five weeks, showed the markedly shortened sternomastoid seen in the photograph reproduced in the article. No improvement following massage, the middle third of the muscle was excised at the age of 6 weeks. This was pale and hard like a fibroma, also the superficial and middle layers of the cervical fascia around it appeared denser. A transverse section showed normal muscle fibres towards the outer side, the remainder more or less atrophic and separated by densely fibrous scar tissue. No remains of blood-pigment were seen.

Four months later there was an extensile band thicker than a lead pencil in place of the excised muscle, and the wry-neck had been quite removed.

*Case IX.* A primipara aged 28 with a normal pelvis had been delivered without difficulty of a female child which had presented by the breech. Three weeks later the mother noticed the right torticollis. Massage and turning of the head failing, the muscle was exposed when the child was aged 8 weeks. The superficial layers of the muscle showed no changes and were simply cut across; the deeper part was throughout the whole length of the muscle changed into hard cicatricial tissue. This part was cut out whilst avoiding injury to the spinal accessory nerve. The excised piece showed a fibrosis with atrophy of muscle most marked in the deeper portion of the muscle. No blood-pigment was noted. The wry-neck was relieved, an extensile band remaining.

*Case X* was very similar to Case IX.

*Case XI.* A woman of 30, at the end of her third pregnancy, with the foetus in a right dorso-anterior transverse position, was delivered by turning and extraction by the feet. The placenta had formed a girdle constricting the lower segment of the uterus, and there had been little amniotic fluid. The child had right torticollis with the concomitant conditions; the right shoulder had been pushed into the neck, the elbow being fully extended and rendered stiff, along with temporary paresis of the upper extremity from compression of the brachial plexus. The contraction of the sternomastoid was overcome by massage and movement.

*Case XII,* in which the child presented by the breech was one of right-sided wry-neck, which was also cured by massage and movement.

*Case XIII.* A woman aged 32, in her second pregnancy, was delivered of twin children, the first, a head presentation, spontaneously, the second a right dorso-anterior transverse presentation by turning. The latter infant had right torticollis which increased after birth, so that at the age of 6 weeks the indurated middle third of the muscle was excised. There was found marked degeneration of muscle fibres with fibrosis affecting mostly the deeper aspects of the muscle, the surface of the muscle exhibited some normal fibres.

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## INTESTINAL EXCLUSION

Maisonneuve, in 1844, with the object of avoiding the formation of an artificial anus in cases of intestinal obstruction, originated the idea of excluding a portion of the intestine by making a lateral anastomosis. Senn, in experiments on animals, divided the ileum and implanted the proximal end into the colon, whilst he closed the distal end. Salzer, as a result of animal experiments, proposed the exclusion of a portion of gut, after restoring continuity of the rest of the bowel, by closing the upper end of the excluded gut and suturing the lower end of the excluded intestine so that it should open upon the surface of the abdominal wall. Trendelenburg, in the case of a cancer of the caecum in which a fistula had already formed, after restoring the continuity of the bowel, closed the two ends connected with the caecum above and below, leaving the faecal fistula to persist in the middle. Other experiments by Vella, in 1882, tested the consequence of stitching both ends of the excluded gut into the abdominal wall, so as to open upon the surface. Denk described the experience over the operation in von Eiselsberg's Klinik, commencing in 1901.

In 9 cases the procedure followed Senn's method, in 3 that of Salzer. The results in the former series were:

*Case I.* For constriction following appendicitis, the division of the ileum, implantation of the proximal end into the sigmoid flexure and closure of the distal end. The patient was quite well 16 years later and had no difficulty with his motions.

*Case II.* For tuberculosis of the caecum was operated upon in the same way; there was temporary relief until death 2½ months after the operation.

*Case III.* Similar to the preceding one, the ileum was joined to the transverse colon. A local abscess was incised six months later and death occurred from tuberculosis two years after the anastomosis.

*Case IV.* Also tuberculosis of the caecum; was first treated like the foregoing and three months later the excluded bowel, including the diseased part, was excised and the patient cured.

*Case V.* A fistula had formed after excision of a piece of the ileum. The operation was done, but the patient died half an hour later from shock.

*Case VI.* Had both a faecal and urinary fistula, the one involving the descending colon, the other the left ureter. In addition to the operation as before, the fistula into the descending colon was closed and the left kidney removed. The patient recovered from the operation.

*Case VII.* Tuberculous adhesions constricted the transverse colon for which ileosigmoidostomy with closure of the distal end of the divided ileum was first tried. Faeces collected in the occluded gut, for the relief of which three further operations were done, ending in complete removal of the intervening ileum and colon.

*Case VIII.* A carcinoma of the caecum for which ileosigmoidostomy was done recovered from the operation, but there was no further report.

*Case IX.* An anastomosis was first done between the ileum and transverse colon, then between the ileum and rectum with closure of the distal end of the divided ileum, in order to relieve ulceration of the caecum. The second operation was fatal from leakage at the line of suture.

*Case X.* There was a cancer of the caecum which had already perforated externally and also into the bladder. The ileum above and the transverse colon below were divided, the proximal end of the ileum being anastomosed with the distal end of the colon; the distal end of the ileum was brought to the surface, the proximal end of the colon closed. Death followed from leakage at the line of suture.

*Case XI.* There was ileo-caecal tuberculosis with a faecal fistula. The operation was similar to the preceding case except that the distal end of the ileum was also closed, and after eleven months the excluded portion was excised. The patient died five months later from perforation of a tuberculous ulcer of the ileum above the anastomosis; there was also generalized tuberculosis.

*Case XII.* For a similar case to the above, first appendicostomy and ileo-colostomy was performed, leaving a faecal fistula. Next the ileum and ascending colon were excluded and the four divided ends closed, still leaving the fistulous opening into the caecum discharging muco-pus. Subsequently, owing to further tuberculous ulceration and communication, a faecal fistula was re-established and death followed eleven months later.

Denk added the following collections of cases. Of 68 cases of entero-anastomosis for tubercle, 6 appeared cured, 6 importantly improved, and 27 deaths followed the operation. The inherent danger following the operation was the distension of intervening coils by faeces and gas, tending to cause perforation and fatal peritonitis. Of 38 cases of carcinoma submitted to entero-anastomosis, 13 died after the operation, and 19 within the following 2–8 months, 2 were still alive and suffering 14 and 15 months respectively after the anastomosis, 1 died 7 years later, the growth proving to be a round-celled sarcoma of the transverse colon. Of 4 there was no further report after recovery from the operation. In 18 cases a lateral entero-anastomosis was done for inflammatory conditions other than tuberculous—constrictions, kinks, adhesions, and faecal fistulae. 5 died of the operation following pre-existing intestinal obstruction and peritonitis. Of the survivors only 1 was proved to be well following an entero-anastomosis for Hirschsprung's disease. 5 in which the operation had been for obstruction, the result of adhesions, had intermittent trouble from collections of faeces in the intervening loop. Of 2 cases in which the entero-anastomosis was done for faecal fistula, one underwent excision and died, in the other the anastomosis failed to cure the fistula.

In contrast with the foregoing, the plan of bringing the two ends of the excluded gut to the surface, and irrigating through it for a time offers definite advantages.

Finsterer reported the experience gained in Hochenegg's Klinik in Vienna. Starting from the experiments by Valla in 1882, of Hochenegg in 1891, and his own in 1916, Finsterer arrived at the decision that the two ends of the excluded gut should be fixed so as to open upon the abdominal wall, pending the excision. In support of this conclusion he added 12 recent cases. Lateral anastomosis had failed owing to the accumulation of faeces in the intervening gut. When an end to end anastomosis was made, and the two ends of the excluded gut dropped back, the excluded gut became distended with muco-pus ending in fatal perforation. Even if there had previously been a fistulous opening into this segment of the bowel, this did not prevent the collection. If the proximal end of the excluded gut were closed and the distal end brought out to open on the surface, there took place an accumulation in the proximal end above the original site of constriction, so that perforation occurred in the proximal end. When the proximal end was kept open and the distal end closed, perforation at the distal end was inevitable.

*Case I.* An infantry soldier, aged 23, had an appendix abscess incised. A faecal fistula followed, so six months later an anastomosis was made between the ileum and transverse colon, and the excluded ends, after temporary closure, were fixed into the abdominal wall. 24 hours later the two ends were opened and tubes inserted for daily irrigation. After three months, the patient having much improved meanwhile, the excluded caecum and ascending colon were excised and the patient discharged well.

*Case II.* A Bosnian, aged 29, had tuberculosis of the caecum complicated by pulmonary tuberculosis. The caecum formed a mass the size of the fist with tuberculous mesenteric glands, and excision was out of the question. The operation as before, followed by daily irrigation, brought away pus and prevented further abdominal trouble until death, two months later, from the pulmonary disease.

*Case III.* An infantry soldier had a faecal fistula in the ileo-caecal region with necrosis of the ilium following a gunshot wound. 5½ months later an attempt to close the fistula and remove the necrosed bone made things worse. 19 months after the wound a second attempt to close the fistula likewise failed. 23 months after the original wound the exclusion operation was done, but previous to this the patient had developed signs of pyaemia, suppuration extended from the ilium through the sciatic notch into the thigh, and was also present in the wrist-joint, and pulmonary abscesses followed, which caused death two months after the exclusion.

*Case IV* was like Case III, but the exclusion operation was done earlier, viz. 7 months after the wound. Irrigation reduced the discharge from the ileo-caecal fistula to a little muco-pus. 14 months after the wound, the excluded gut was excised, and the fistulous track scraped and drained. The patient was discharged after two months much improved, the track of the fistula having become reduced to a small sinus.

*Case V.* In a man aged 46, carcinoma of the hepatic flexure of the colon had become complicated by a faecal fistula. The exclusion operation being done, daily irrigation reduced the suppuration so that 5 weeks later the excluded gut and the cancer were excised. 22 months later the man was in full work and free from recurrence.

*Case VI.* A man aged 50 underwent 7 operations on account of cancer of the lower end of the sigmoid flexure. (i) October 1917. Left inguinal colostomy for the relief of acute intestinal obstruction. (ii) December 1917. The cause being overlooked, an attempt was made to close the colostomy and acute obstruction recurred. (iii) The wound being re-explored, the ileum was opened, so that a faecal fistula formed; the bowel emptying, the cancer was discovered and an additional opening made into the caecum. (iv) February 1918. The cancer of the sigmoid was removed along with the descending colon, the lower end of the sigmoid was closed and transverse colostomy instituted, with closure of the fistula in the ileum. (v) May 1918. Again intestinal obstruction was relieved by separating adhesions between the ileum and the abdominal wall. (vi) May 1918. Union of the ileum to the sigmoid, leaving a fistula communicating with the excluded caecum. (vii) June 1917. A partial removal of the excluded gut was abandoned on finding extension of the cancer to the lymphatic glands and peritoneum. Just a year after the first attack acute intestinal obstruction recurred causing death. Perforation had occurred at the site of the ileo-sigmoid anastomosis following enlargement of mesenteric glands.

*Case VII.* A man aged 25 had an appendix abscess incised in February 1917, and a faecal fistula followed. In May 1918 the excluding operation was done and as a result of the irrigation the fistula soon closed. In November 1918 the excluded gut, which had become much more mobile, was easily excised and the man discharged well eight weeks later.

*Case VIII* was a similar case. The appendix abscess was incised in January 1918 and a faecal fistula followed. The exclusion operation was done in October 1918, the excision following irrigation a month later, and the man discharged well in February 1919.

*Case IX* had tuberculosis of the caecum, which formed a mass the size of the fist. After exclusion, followed by irrigation for five weeks, the caecum perforated into the peritoneum and death followed.

*Case X* was wounded by a shell in the right loin in September 1918, and like Cases III and IV had a faecal fistula with necrosis of the ilium, In June 1919 the exclusion operation was done, when, after irrigation, the faecal fistula closed, whilst the opened ends of the excluded gut discharged only a little muco-pus.

*Case XI*, with tuberculosis of the caecum and pulmonary phthisis, had exclusion done in July 1918. The patient improved so markedly under irrigation, that in February 1919 excision was done, but he died two days later with signs of pneumonia.

*Case XII.* A faecal fistula had followed strangulated right femoral hernia and persisted for two years. After the exclusion operation there was improvement, but the fistula continued to discharge a little muco-pus.

Mercadé reported the following case. A girl aged 16 had an appendix abscess incised in December 1915, and in January 1918 she presented several fistulae in the right iliac fossa by which the whole of the intestinal contents were discharged. On exploration the end of the ileum was found dilated and the colon beyond the fistulae reduced to the calibre of the little finger. An end to end ileo-sigmoidostomy was done, and the ends of the excluded gut closed, leaving the fistulae open. The following day the patient passed motions by the rectum for the first time for more than two years. In the following month, February 1918, the ileo-caecal segment with the fistulae was cut out, the proximal end of the ascending colon closed, the distal end of the pelvic colon fixed into the lower end of the incision. Healing followed, a discharge of mucus only continuing from the open distal end. In August 1918 the remaining colon was excised and the patient at the time of the report was in excellent general health, had grown fatter, had solid motions, and but two a day. If, as recommended by Finsterer, both ends of the excluded gut had been brought out, irrigation might have rendered the ileo-caecal part of the excision easier, and the rest of the colon might then have been taken away at the same time.

**Finsterer, H.** Ein weiterer Beitrag zur totalen Darmausschaltung. *Deutsche Ztschr. f. Chir.*, 1920, **155**, 145.

**Denk, W.** Ueber ausschaltende Operationen am Darm (Von Eiselsberg's Festschrift). *Arch. f. klin. Chir.*, 1918, **110**, 131.

**Mercadé, S.** Iléosigmoïdostomie termino-terminale suivie de colectomie (rapport de Okenczye). *Bull. et mém. Soc. de chir. de Par.*, 1921, **47**, 160.

W. G. S.

# THE PHYSIOLOGY OF THE ELEMENTARY NERVOUS SYSTEM: ITS BEARING UPON SOME MODERN NEUROLOGICAL PROBLEMS

It has been aptly said that the edifice of the whole nervous system is reared upon two neurones, the afferent root cell and the efferent root cell. These are the pillars of the fundamental reflex arc, upon which all the other neural arcs are superimposed, even those of the cerebral cortex. It is with the development of these anatomical and physiological foundations of the nervous system, in those simple animal forms in which they first make their appearance, that Parker deals in his book on *The Elementary Nervous System.* Beginning with the sponges, in which contractile muscle-tissue develops as an independent effector organ before any nervous elements have been differentiated, Parker passes to the coelenterates—hydrozoa, sea anemones and jelly-fish—in which there is a receptor-effector system consisting of sensory and motor elements with their appropriate receptor and effector organs. In his concluding chapters, he describes the earliest manifestations of centralization in the diffuse nerve-net of these primitive animals, and the appearance of internuncial nerve-cells placed between sensory and motor elements.

Not only does he deal with the morphology of this primitive neuromuscular mechanism, but also with its modes of response. This physiological aspect of the question is perhaps of even greater interest and importance to the neurologist than the purely anatomical. At the present moment there is a great need for accurate and extensive observation upon the nature of the reactions characteristic of the elementary nervous system, and this for reasons which call for some preliminary explanation.

**Dissolution of function in disease of the nervous system.** Within the past few years, the systematic investigation of the phenomena of nervous disease has thrown considerable light upon the functions of this system, and upon the manner in which disease disorders them. Clinical neurology in this country has never been satisfied by the mere description and classification of the symptoms of disease, but has always attempted to interpret these in terms of disordered function, and by their study to throw light upon the physiology of the nervous system. In this way many notable advances have been made, as, for example, in our knowledge of the problems of sensation and of the co-ordination of muscular movement. Nevertheless, many problems await solution, and probably many more have yet to be recognized.

It is in respect of certain hypotheses concerning the evolution of function in the nervous system, and based upon clinical observations, that the investigations made and so admirably recounted by Parker promise to be of the greatest value.

These hypotheses are founded upon a general principle enunciated by Hughlings Jackson many years ago, to the effect that, for purposes of investigation, nervous disease might be regarded as a reversal of evolution, that is, as a dissolution, in which function is 'taken to pieces' in a definite fashion; the highest and most recently acquired activities being earliest and most severely affected, the lower, more automatic and more deeply organized activities being more resistant. Further, such a dissolution being partial—

when death does not ensue—the symptomatology of nervous disease must be dual; there will be a negative or defect symptomatology due to loss of function in the centre destroyed or inactivated, and a corresponding release from control and unbalanced activity of subordinate centres which remain intact. In other words, disease dissects out the functional components of the activity of the nervous system, and from the study of the lower levels of evolution remaining, light may be thrown upon the gradual evolution of function in the nervous system.

Fruitful as this guiding principle has been, there is clearly a danger that it may be laboured, that it may be applied beyond its capacity in the endeavour to determine the physiological meaning of symptoms. For example, the hypothesis makes no provision for qualitative alterations of function, or perversions of function. To apply it universally means that we accept defect and release as a complete explanation of all the symptoms of disordered function that we see in nervous disease. Surely this is an assumption we have no right to make. Be this as it may, the principle is widely accepted as universally applicable, and certain important corollaries have followed from this.

The one with which we are now concerned is that this supposed dissolution of function unmasks earlier phases in the evolution of nervous activity. Thus, in their well-known work on peripheral sensation, Head and Rivers maintain that the 'protopathic' sensibility remaining at the periphery of a denervated area of skin, and present throughout this area at the end of the first stage of regeneration, represents a primitive form of sensibility; disease or injury has dissected normal cutaneous sensibility into two physiological components of widely differing capacity and far removed in phylogenetic origin. Similarly, the reflex activity of the isolated segments of the divided spinal cord in man have been regarded as representing primitive motor activities released from higher control and reappearing in their primitive form (Head and Riddoch). In other words, in protopathic sensibility and in the 'mass reflex' of spinal man, we see approximations to the sensori-motor reactions of a primitive animal. In his recent book, *Instinct and the Unconscious,* Rivers has fully expounded this biological aspect of the subject and has summed it up in the following words: 'All we know of the protopathic stage is consistent with its being the representative of the sensibility of an animal which possesses only the power of becoming aware of changes of a crude kind and, according as these changes are pleasant or unpleasant, of reacting at once by such mass-movements as would take it nearer to, or remove it from, the source of stimulation'. (Rivers, p. 23.)

How far do the facts of observation, as recorded by Parker, confirm this view? Clearly they should afford us a valuable means of assessing the significance of the phenomena described by Head and his co-workers, and further, of deciding whether the Jacksonian principle, upon which their conclusions are based, can be safely applied to all the phenomena of nervous disease.

**The 'protopathic' animal.** With this end in view, let us briefly examine the sensori-motor endowment of the hypothetical 'protopathic' animal. *Protopathic sensibility* is a high-threshold form of cutaneous sensibility, responding solely to pain and to extremes of temperature. (Head, Rivers and Sherren, p. 63.) It carries no power of localizing a spot stimulated; no power of appreciating intensity of stimulus, for the sensations perceived are of the 'all-or-none' kind; there is no power of determining the nature of the stimulating object, beyond the fact that it may convey a pleasant or unpleasant feeling tone ; sensations radiate widely and are often erroneously localized at a considerable distance from the spot stimulated. In short, to use Rivers's words, protopathic sensibility contains 'elements of vagueness and confusion quite incompatible with the exact power of localization. . . .' (Rivers, p. 30.)

To what type of reaction does this extremely strange and restricted form of sensibility lead ? Head and Riddoch observed that after division of the spinal cord, the isolated portion, having emerged from the state of spinal shock, shows an intense reflex activity. They discerned in this many points of resemblance to protopathic sensibility. Thus, 'the situation of the stimulus does not determine the distribution of the response ; local signature is abolished, and the outburst of energy flows into channels that would be blocked under normal conditions'. (Head, p. 753.)

The reflex response invariably obtained under these circumstances consists of powerful bilateral flexion of the legs, contraction of the abdominal muscles, evacuation of the bladder, and an outburst of sweating. This is elicited by all forms of stimulation applied anywhere below the level of the cord lesion, to skin or to deep structures. The response is stereotyped in form and unvarying in intensity. Should the stimulus be gentle friction of the glans penis, bladder evacuation is replaced by erection and seminal emission. This type of '*mass reflex*' has been called 'the coitus reflex'. Apart from this single exception, 'all local adaptation to the site or nature of the stimulus is swept away in a violent outburst of energy in centres cut off from higher control'. (Head, p. 753.) And again, 'a reaction of this kind is admirably fitted to defend the animal from noxious influences; it produces movements of withdrawal, which permit of no choice'. (Head, p. 752.) Finally, and scarcely consistently, 'both the segmental and the massive response are means of defence and lead to withdrawal of the part from noxious influences. But they hamper voluntary action by the uncontrolled movements they evoke, and tend to prevent escape by fixing the body in a position unfavourable for flight. The animal crawls into a hole to die or to recover . . .' (Head, p. 753.) The 'mass reflex' is said to represent the reappearance 'in its primitive form' of an elementary motor mechanism normally kept under control.

It is very difficult to regard this chaos of reflex responses as anything but a pathological demonstration of what might aptly be called spinal anarchy. The protopathic animal, in response to a stimulus which it cannot localize, which has but a single intensity and gives no information as to the nature of the stimulating object, makes a response which consists of profuse sweating, bladder evacuation, and powerful tonic flexion of the hind limbs, or squatting. The primitive animal thus endowed would be an organism utterly unfitted to cope with its environment. So helpless and bewildered a creature could not survive long enough to perpetuate its race, even if it could make an effective effort to do this, and with its appearance the process of evolution must almost inevitably have ceased.

These reflections are forcibly suggested by the biological consequences of this theory of the dissolution of function. Let us see what actual observations upon the physiology of the elementary nervous system have to say on this point.

**The elementary nervous system.** In the case of such a primitive animal form as the jelly-fish, or the sea anemone, we can determine the presence of graduation and localization of sensation only by a close study of the characters of the response. In these animals there are several forms of effector organ, but of these only the muscle is under nervous control. We must therefore study the motor responses of these animals.

If the sea anemone *Metridium* be stimulated at any point by a glass rod, the whole musculature of the animal goes into strong tonic contraction. If, however, we employ physiological stimuli, finely graded motor reactions may be observed. 'If a Metridium be allowed to remain for some time in running sea water in a situation relatively dark, its muscular tonus will be reduced to a minimum, and it will assume the condition of fullest normal expansion. If, under such circumstances, it is generally and briefly illuminated, it will quickly shorten its length quite noticeably, though it will by no means go into what would be described as a state of contraction. This shortening of the animal as a whole is due to the simultaneous moderate contraction of its longitudinal mesenteric muscles. The fact that the shortening is symmetrical and uniform shows that a complete ring of these muscles has contracted in unison. If, instead of subjecting the fully expanded sea anemone to a general illumination, light is thrown on only one of its sides, it responds usually by turning its oral disk toward the light, precisely as some flowers come to face the light . . . hence the nerve-net exhibits under a more normal form of stimulation a type of response much more delicate in character than what is seen when a glass rod is used.' (Parker, p. 100.) Finally, Parker concludes that the responses of such an animal are not of the 'all-or-none' character, but are finely graded according to the strength and the site of the stimulation.

The response of the tentacles to stimulation show the same features as those of the musculature of the wall of the organism. (Parker, p. 122.) Further, according as we stimulate the tentacles of the sea anemone with either weak acid or with fish meat, so the whole nature and site of the response differs completely.

Finally, in the tiny polyp *Corymorpha,* Parker has observed the following delicately localized and graded response to localized stimuli (p. 189): 'If a faradic stimulus is applied to one side of the stalk next the hydranth or next the base, the stalk simply shortens as a whole. If, however, the stimulus is applied to one side of the stalk nearer the middle of its length the stalk bends to that side and usually presses the hydranth with great accuracy against the stimulated spot. This response is not only appropriate for the particular side stimulated, but also in most cases for the given level of the stimulated spot on that side. The significance of these responses to localized stimulation were often observed in the stock aquarium. This contained by accident a number of small nudibranch gastropods, which were found to feed upon the substance of *Corymorpha.* When one attacked a *Corymorpha,* it began near the base of the stalk where the hydroid rose from the mud, and as soon as it started to nibble the stalk on a given side the *Corymorpha* responded by applying to the point of attack the hydranth, the tentacles of which were extremely stimulating to the nudibranch and usually drove off the intruder. *The success of this form of protective response naturally depended upon the accuracy of the localization.* . . . This accurate form of response of a distantly located organ to a circumscribed stimulus has all the characteristics of a reflex. . . .'

**Differentiation and integration.** Therefore, it seems that from its earliest origin, the nervous system is capable of assuring a perfect though simple co-ordination. Sherrington has emphasized that a simple act of co-ordination may be as perfect as a highly complex one, and that, as differentiation of the organism takes place, the integrative activity of the nervous system keeps pace with this differentiation. The so-called 'crude' forms of activity, which Rivers supposes the elementary nervous system to possess, are nowhere to be observed throughout the animal kingdom, whether we study jelly-fish, insects, or man. Indeed the use of the word 'crude' in this connexion is greatly to be deprecated. It means almost anything and therefore defines nothing, and it has no more place in biology than that quaint figment 'the protopathic animal', whose nervous system it describes. The elementary nervous system may be simple and limited in its range of action, but crude never.

Indeed, it seems clear that in respect of insect behaviour Rivers is conscious of some discrepancy between his hypothesis and the observed facts, and he assumes that the finely discriminated and graded reactions of insects must have been derived from 'originally crude modes of response' under the influence of some unknown 'graduating mechanism' (p. 50). We cannot refrain from asking whether this way of looking at things is likely to lead us any nearer to a solution of these interesting problems. We can find no reason for these two assumptions, unless it be the requirements of an hypothesis which is not in accord with the facts. Surely, a more promising line of advance would be rather to study the reactions of the elementary nervous 'system and to base our theories on what we observe, than to roll this academic hypothesis before us, Sisyphus-like, in our efforts to attain objective truth.

To these principles which Sherrington has emphasized, and to these facts of observation, the whole conception of protopathic forms of sensibility and motor reaction runs directly counter. What is of even greater importance is that this wide diversity between the hypothesis of Head and his co-workers in this respect and what we actually know of the elementary nervous system, shows that the Jacksonian principle is a fallible instrument if it be employed as a universal law, which Jackson surely never intended, instead of as a working hypothesis to be used with discrimination. In our future interpretations of the symptoms of disordered nervous function, we shall have to take account of the probability that function is sometimes qualitatively altered or perverted in a fashion not to be explained along these simple lines.

[The page numbers in the references to the papers of Head and his collaborators are from the collected *Neurological Studies*, and not as in the original papers in *Brain*.]

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F. M. R. W.

# ABSTRACTS

## NEUROLOGY

**Draper, G. Acute poliomyelitis.** *William Heineman, London,* 1917.

The fortunate circumstance that these islands have never been ravaged by severe epidemics of acute poliomyelitis has deprived observers in this country of the extensive opportunities, which the outbreaks of the disease in the United States have afforded observers there, of studying the acute initial stages of the disease. There appears to be nothing sufficiently characteristic of the acute systemic phase of this to render it recognizable when none but sporadic cases occur.

Although the well-known Rockefeller monograph of 1912 and Batten's Lumleian lectures of 1916 (*Brain,* 1916, **39**, 115) summarized our knowledge up to the latter date, yet Draper's account contains a more detailed description of the initial symptomatology of poliomyelitis than has yet been available in this country, and will therefore be read with interest.

A striking feature revealed by the study of the disease in epidemic form has been the large proportion of cases which never develop paralysis. This fact has been known for some years, and has been completely borne out by the American epidemics of the last five years. Draper places the proportion of non-paralysed cases at 50 per cent., and quotes other authorities who place it as high as 70 per cent. and 80 per cent.

It follows from this that the terms ' abortive type ', ' infantile paralysis ', and ' poliomyelitis ' applied to this disease are not accurate, since the acute systemic phase of the disease is not necessarily accompanied by any involvement of the nervous system. Further, any classification based upon the incidence of the paralysis fails to include at least half of all recognized cases. Since both paralysed and non-paralysed cases show the same initial systemic symptom-complex, he proposes a basis of classification according to the characters of this phase of the disease.

The acute or active stage of poliomyelitis consists of two phases : *a first phase of general toxic-infection,* which ends either in recovery, or is succeeded by *a second and distinct phase of nervous involvement.* It appears that death in this disease is never due to toxaemia, but to direct involvement of the nervous mechanisms of respiration. Hence, death never occurs apart from the development of the second phase.

**The first phase—general toxic infection.** This is invariably febrile, and lasts from 24 to 48 hours. It may be followed by a complete remission and apparent recovery of the patient, but after an interval of from 3 hours to several days, paralysis suddenly appears and ushers in the second or nervous phase. On the other hand, no such remission may occur, and the first and second phases may be continuous. For these two variations, Draper has employed the somewhat fanciful terms 'dromedary type', from the occurrence of two 'humps' of symptoms, and 'straggling type' respectively.

The symptoms accompanying the fever and constituting the clinical picture of the systemic phase are not in themselves particularly characteristic of poliomyelitis. They vary in different epidemics, and in different foci in a single outbreak. They may be predominantly (*a*) gastro-intestinal, when diarrhoea is a prominent symptom; (*b*) tonsillar, or (*c*) upper respiratory, or (*d*) pains and malaise may be the only definite symptoms noticed. Whatever form the symptoms take, they vary in intensity from case to case.

In the early hours, the clinical picture resembles that of any other acute specific fever of childhood. The child is dry, hot, and restless. When gastro-intestinal symptoms are prominent, the case may be taken for simple summer diarrhoea. It is important to remember that these symptoms are not prodromata of the disease, but the manifestation of the fully developed general infection itself.

Draper states that observers seeing cases during an epidemic soon learn to appreciate trifling and subtle clinical features, by which they can often detect the nature of the illness. Other common symptoms are pain and tenderness of muscles, congestion and soreness of the fauces, and enlargement of the lymphatic glands. While diarrhoea is common during the first phase, after nervous involvement has appeared, constipation is the rule.

**The phase of nervous involvement.** The degree of nervous disturbance varies from a mild and transient meningeal reaction to widespread paralysis and death. It is difficult to determine, from the character and severity of the symptoms during the first phase, whether paralysis is likely to ensue. As we have seen, a complete remission of symptoms may intervene between the first and second phases of the acute disease, but, nevertheless, there are commonly both clinical and other indications of invasion of the meninges by the virus before paralyses appear. Among these is the 'spine sign'. This consists in rigidity of the spine, passing sometimes into opisthotonos. Its appearance, or its sudden increase, during the early hours of the illness is a reliable indication that the nervous system is beginning to be invaded. Other manifestations are sudden and transient changes in the tendon-jerks, increased muscular pain, and headache. Repeated lumbar punctures during this period reveal the meningeal reaction which underlies these symptoms. During the early hours, and when no meningeal symptoms are present, the cerebrospinal fluid is found to be under pressure, but contains no abnormal increase of cells or of globulin, but with the appearance of meningeal symptoms, sometimes without these, the fluid shows an increasing cell content. At first, and in severe cases, numerous cells resembling polymorphonuclears are seen, but later the cells are exclusively lymphocytes. The content may range from any number over ten per cubic millimetre to over a thousand. As a matter of practical interest, Draper records that if during the first 12 to 18 hours the cell count does not exceed 100 per c.mm. paralysis is not likely to follow.

However, prognosis during the preparalytic period is difficult, since the nervous symptoms of the second phase may be as trivial and transient as those of the first.

Clinically, cases passing on to a phase of nervous involvement may be classified as follows: (1) transient meningeal reaction with recovery; (2)

stupor followed by transient facial paralysis and recovery; (3) transient limb or trunk paralysis; (4) persistent paralyses with slow and partial recovery; (5) fatal cases in which the nuclei of the intercostal and phrenic nerves, or the respiratory centre in the medulla, are involved. In these the paralysis may be ascending or otherwise progressive.

While motor nerve-cells in brain-stem or cord are most commonly involved, it is known that the upper motor neurones may also be attacked, with the production of true encephalitic types, with hemiplegia and convulsions.

**Treatment.** In the general management of a case, Draper insists on isolation not only of the case itself, but, for a period of ten days, of the rest of the family. The occurrence of cases without ensuing paralysis makes efficient quarantine in an epidemic impossible, for these cases are the most active spreaders of the disease. During an outbreak, it should be remembered that both nasal secretions and faeces are infective, and possible carriers should be particularly careful to see that their hands are kept as clean as possible in these respects. During the most recent outbreak of the disease, the use of *serum treatment* began to come more extensively into use, but it has not yet been developed on a large scale. Experience, both experimental and clinical, shows that immune serum from a recovered case is more likely to protect the nervous system if administered before, or early, in the meningeal invasion period. Before there is any sign of meningeal invasion, intravenous or subcutaneous injection of serum from a recovered case is advocated, but once signs of meningeal invasion have appeared, intrathecal injection is preferable. During an epidemic it should be easy to obtain the required serum, but for cases occurring sporadically there will probably always be considerable difficulty in hurriedly obtaining an immune serum, in excluding syphilis in the donor, and in injecting it before paralysis has developed—if diagnosis is possible before this—or within a few hours of its appearance. So that, in the conditions under which poliomyelitis is seen in this country, serum cannot yet be considered a potent weapon in the hands of the physician.

If there is any fault to be found with Draper's valuable account, it is that the wealth of information it contains is unsystematically arranged. The use of metaphorical terms, such as 'dromedary' and 'hump', cannot replace lucidity of expression, or system in arrangement. Indeed, the physicians of fifty years ago, who gave us such living and vivid accounts of the diseases they described, never found it necessary to eke out their vocabulary by the adoption of far-fetched zoological metaphors of this kind.

F. M. R. W.

**Levaditi, C., et Harvier, P.** Étude expérimentale de l'encéphalite dite léthargique. [**An experimental study of so-called lethargic encephalitis.**] *Bull. de l'Inst. Pasteur*, 1920, **34**, 911.

From their experimental studies, Levaditi and Harvier have arrived at the following conclusions:

1. That the virus of encephalitis is pathogenic for the rabbit and for the guinea-pig, but little or not at all for the monkey.

2. The symptomatology and pathology of the experimental form of the disease closely resembles the disease as seen in man.

3. The causative agent is a filterable virus, which lives for 48 hours

after death of the infected animals, persists in glycerine, but is killed by prolonged contact with phenol at 100° C.

4. The rabbit can be successfully inoculated through the eye or the peripheral nerves, but not through the skin, the blood-stream, the peritoneum, the air-passages, the intestinal canal, or the salivary glands.

5. The intact nasal mucosa resists the invasion of the organism unless it is inflamed or damaged. In the latter circumstances the virus probably travels along the olfactory nerve filaments to the brain.

6. The virus is found in the brain and cord, but not in the blood or cerebrospinal fluid, or in the viscera, including the salivary glands. It is excreted via the nasal mucosa, which it probably reaches along the olfactory nerve filaments from the brain.

7. In man, infection probably occurs through the nasopharynx.

8. The experimental disease does not clear up spontaneously, hence there is no subsequent period of immunity, but a certain degree of artificial immunity can be conferred by vaccination with live or dead virus.

9. The serum of convalescents and of vaccinated animals has no protective properties, or bacterial action on the virus.

10. Experiment and minute histology suffice to differentiate this disease from acute poliomyelitis. Neither of these diseases confers immunity for the other.

11. Certain cases of acute febrile chorea are due to the virus of lethargic encephalitis.

12. There are attenuated varieties of the virus, and these can be kept alive *in vitro* in symbiosis with cellular elements. F. M. R. W.

**KALBERLAH, F.** Zur Aetiologie der multiplen Sklerose. [**The aetiology of disseminated sclerosis.**] *Deutsche med. Wchnschr.*, 1921, **47**, 102.

Kalberlah inoculated rabbits intradurally and intraperitoneally with blood and cerebrospinal fluid from two active cases of disseminated sclerosis. One of the inoculated animals developed paralyses, and from its blood during life a spirochaete was obtained. A second animal inoculated from this also developed paralyses, but its blood revealed no spirochaete.

The rabbit inoculated from the second case died within two weeks and the expressed liver juices, when stained by Giemsa's method, showed a spirochaete similar to that found in the first case.

The organism is plumper than *S. pallida*, and tapers to a point at each end. It has from three to six spirals. Neisser and Klein examined Kalberlah's preparations and confirmed his observations.

Healthy rabbits and animals dying from other causes in the cages did not show a similar organism.

Kalberlah names it *Spirochaete polysclerotica*, and considers it to be in all probability the cause of disseminated sclerosis. F. M. R. W.

**PARKER, H. L. Juvenile tabes: review of the literature and summary of seven cases.** *Arch. Neurol. & Psychiat.*, 1921, **5**, 121.

In a review of the literature, Parker finds that tabes is the rarest form of syphilis of the nervous system in children. Meningovascular syphilis and general paralysis are both more common. On the whole, girls seem to be more frequently affected than boys; in this respect the juvenile form is in striking contrast to the adult form. The average time of onset is the period of puberty. The parents usually show a positive Wassermann reaction, and the frequency with which the parents of juvenile tabetics are themselves either tabetics or paretics, seems to confirm the view that there is a neurotrophic strain of syphilitic virus, as the French observers believe.

The course of the juvenile form is remarkably protracted and is not infrequently complicated in the later stages by the mental changes of general paralysis. In this way many cases probably escape recognition.

Any of the symptoms of the disease as it is seen in adults may occur in the juvenile form, but on the whole the latter has a symptom grouping of its own.

The onset is very insidious and the most constant early symptom appears to be incontinence of urine. The next most frequent is optic atrophy, which is found sooner or later in the great majority of cases. The characteristic pupil changes of tabes are also seen in juvenile cases, but ocular palsies and diplopia are rare. Headache is a very common symptom, and although lightning pains occur, they are perhaps not so constant or so severe as in adult cases. Girdle pains and gastric crises are also less common. The objective sensory changes are like those of adult tabes, but are apt to be less extensive. The knee-jerks are lost in the great majority of cases, but ataxy is a symptom of exceeding rarity.

Parker analyses seven observed cases, which he studied in the Mayo Clinic to which he is attached. He notes a feature not recorded in the literature, namely, well-marked hypotonus. In four, the pupils were completely immobile, and mydriasis was the rule. In all, the course was slow.

F. M. R. W.

**Naccarati, S. The oculo-cardiac reflex (Dagnini-Aschner phenomenon)—its use in medicine and psychology.** *Arch. Neurol. & Psychiat.*, 1921, **5**, 40.

Described by Dagnini and Aschner independently in 1908, the phenomenon consists in slowing of the pulse, lowering of the blood-pressure, and alteration of the rhythm of respiration on compression of the eyeballs.

Experimental observations indicate that the phenomenon is a true reflex, the afferent path of which is the fifth nerve, and the efferent path the vagus and possibly also the cervical sympathetic.

The reflex has been widely used on the Continent as an empirical sign in various nervous diseases, but with conflicting results, except possibly in the case of tabes in which it is universally found to be absent.

The standard commonly accepted as normal is a slowing of from five to twelve beats per minute in the pulse-rate. Greater slowing is regarded as an exaggerated response, less as a diminished response.

To obtain the reflex, the patient is placed in the recumbent posture or lying back in a chair. When the pulse-rate has become constant, the eyeball is compressed through the closed lids by the thumb and index finger of the right hand. The pulse-rate at the wrist is simultaneously taken by the observer. Naccarati finds great variations in the same individual at different times, hence the difficulty in establishing a normal standard, and he suggests that the difference between the pulse-rates should be recorded with and without pressure, with a plus or minus sign. This figure he calls the reflex index; thus a slowing of twelve beats per minute is recorded as +12. Observations were made upon 500 subjects, healthy and abnormal.

Of the normals, 40 per cent. showed a positive index of from 0 to 4. In the remainder the index was variable. A single observation is said to be of little value, and repeated tests are necessary to establish an average.

Naccarati adds a list of factors, both physiological and psychological, which influence the character of the response in normal subjects, and it becomes clear from his observations that the oculo-cardiac reflex has no diagnostic value whatever.

It is unfortunate that he does not say this at once, and thus put in its proper perspective a phenomenon which has cumbered neurological literature unduly. Instead, he goes on to say that 'it may constitute an index of the psychic condition and of the sympathetic-endocrine make-up of the subject, but only when other factors have been standardized. In normal persons the reflex index may serve as an indication of reflex control, moods, courage, emotions, &c., traits whose scales are wanting.' All of which means precisely nothing.

It seems characteristic of the craving for new and bizarre 'signs', for ever fresh empirical diagnostic tricks, that it gives rise to an extensive and unscientific literature, which rises mushroom-like as each new phenomenon is recorded. The quotation given above from Naccarati's paper is typical of the scientific value and general style of the papers in which these new signs and wonders are proclaimed.

The atrocious phrase 'sympathetic-endocrine make-up' is an epitome of this class of neurological literature, to which, fortunately, this country is not addicted.

The therapeutic value attributed to the phenomenon in controlling paroxysmal tachycardia is not dealt with. F. M. R. W.

**de Kleijn, A.**, u. **Magnus, R.** Labyrinthreflexe auf Progressivbewegungen. [**Labyrinthine reflexes to progressive movements.**] *Arch. f. d. ges. Physiol.*, 1921, **186**, 39.

Various progressive reflex movements which are connected with particular spatial movements fail if the labyrinths are destroyed, but persist if the afferent nerves to the muscles concerned are divided, or when either the cerebrum or cerebellum is removed. It is concluded that the centres for such movements dependent on the integrity of the labyrinth are somewhere in the brain-stem. Destruction of the otoliths by centrifugation leaves these reflexes intact; they arise therefore from the semicircular canals and not from the utricle and saccule. The function of the semicircular canals is always concerned with response to acceleration, either angular or rectilinear, as contrasted with the static functions of the maculae and otoliths. C. L. E.

**de Kleijn, A.** Tonische Labyrinth- und Halsreflexe auf die Augen. [**Tonic labyrinthine and neck reflexes of the eyes.**] *Arch. f. d. ges. Physiol.*, 1921, **186**, 82.

Tonus of the eye muscles depends on the position of the head ; (*a*) in space (labyrinth reflexes), and (*b*) with relation to the neck. The latter reflexes persist after bilateral destruction of the labyrinth. As a result of these two types of reflex, the eyes tend to maintain a constant position in space, i. e. an unaltered visual field. C. L. E.

**DE KLEIJN, A., u. MAGNUS, R.** Über die Funktion der Otolithen. I. Otolithenstand bei den tonischen Labyrinthreflexen. II. Isolierte Otolithenausschaltung bei Meerschweinchen. [**On the functions of the otoliths. I. The place of the otoliths in tonic labyrinth reflexes. II. Separate removal of the otoliths in the guinea-pig.**] *Arch. f. d. ges. Physiol.*, 1921, **186**, 6 and 61.

(1) The experiments were carried out in rabbits. The general conclusion, which is not at variance with clinical findings, is that the maculae are sense organs which respond principally to traction. When the otolith is horizontal, and dependent from the macula so as to pull upon it, the impulses set up are at a maximum ; when the position is reversed, so that the otolith lies directly over the macula and presses on it, the afferent impulses from the latter are at a minimum—whether they disappear altogether is undecided. The sensory apparatus and its afferent path, together with the tonic reflexes of position with which it is concerned, appear to be quite incapable of fatigue. Tonic labyrinthine reflexes of the extremities, neck, and trunk are originated in the utricle, and asymmetric postural reflexes in the saccule. The site for initiation of symmetrical postural reflexes may be either or both. Vertical compensatory eye-movements originate from the main saccule otolith, and rotatory ones from the independently innervated angle of the saccule. The experiments, when taken in conjunction with the authors' previous work on the labyrinthine reflexes, give certain indications as to the central connexions of the various branches of the vestibular nerve. Thus the path for tonic labyrinthine reflexes is connected behind the entrance of the eighth nerve with the centres for the muscles concerned, while that for labyrinthine postural reflexes passes to the posture-centres in the mid-brain. The path for the impulses governing vertical compensatory eye-movements is to the nucleus of the superior rectus of the same and inferior rectus of the opposite side, while that for the wheel-movements is to the nuclei of the inferior oblique and trochlearis. There are many good examples of reciprocal innervation in these labyrinthine reflexes. No definite participation of the semicircular canals in these reflexes could be demonstrated.

(2) When guinea-pigs are rotated in a centrifugal apparatus at the rate of 1,000 revolutions per minute for 1 to 2 minutes, the static postural tonus functions of the labyrinth are frequently lost, while the labyrinthine responses to movement are retained. When this happens it is found that the otolith membranes have been detached, while the cristae of the semicircular canals have remained intact. This experiment, in which definite clinical features are recalled, thus supports the belief that the utricle and saccule are concerned with static equilibrium, while the semicircular canals are the corresponding organs for dynamic co-ordination. C. L. E.

## PATHOLOGY AND BACTERIOLOGY

**BLAKE, F. G.**, and **CECIL, RUSSELL L.** **Studies on experimental pneumonia. IX. Production in monkeys of an acute respiratory disease resembling influenza by inoculation with *Bacillus influenzae*.** *J. Exper. M.*, 1920, **32**, 691.

**Cecil, Russell L., and Blake, F. G. Studies on experimental pneumonia. X. Pathology of experimental influenza and of *Bacillus influenzae* pneumonia in monkeys.** *J. Exper. M.*, 1920, **32**, 719.

The important researches on pneumonia by the authors have already been abstracted in *Medical Science* (1920, **3**, 63, 358; 552). The present, their ninth paper, deals with the production in normal monkeys of an acute respiratory disease following the inoculation of *B. influenzae* on the mucous membranes of the upper respiratory passages and of broncho-pneumonia from intratracheal inoculation. One strain of *B. influenzae* was used throughout these experiments and was originally raised in pure culture from the suppurative pleural exudate of a child, the subject of influenzal pneumonia. A preliminary intratracheal test inoculation of a monkey having shown that the microbe was non-pathogenic, an attempt was made to exalt the virulence by passage. This was attained through a series of eleven white mice followed by a series of thirteen monkeys. Large doses were used to begin with, but at the completion of the series a dose of 0·1 c.c. of a 16-hour blood broth culture from the peritoneal exudate of the passage monkey No. 13 killed a white mouse within 48 hours. In the subsequent experiments two species of monkey were used, viz. *Cebus capucinus* and *Macacus syrichtus*. Two methods of inoculation were employed with different purposes in view. In order to find out whether *B. influenzae* would initiate an infection of the upper respiratory passages, material was introduced into the nose either by means of a pipette or by a swab dipped in the culture medium. In a second series the culture was injected directly into the trachea. The clinical history and post-mortem appearances of twelve monkeys treated by the first method of inoculation are carefully given. A respiratory disease was produced of 3 to 5 days' duration characterized by sudden onset with profound prostration, the development of rhinitis and tracheo-bronchitis with cough, sneezing, and the presence of a scanty mucoid or muco-purulent nasal discharge. In five instances suppuration of one or both antra occurred, and in three there was a broncho-pneumonia. Sometimes there was a definite leucopenia. *Bacillus influenzae* was recovered at autopsy from the lesions of the disease and was either in a pure state or associated with micro-organisms known to be normal denizens of the upper respiratory tract of monkeys.

Of ten monkeys injected with cultures of *B. influenzae* into the trachea seven developed broncho-pneumonia, two had tracheo-bronchitis alone, and one was unaffected. The general symptoms and duration of the disease were similar to those observed in the first group of experiments. The authors consider that the experimental disease is, in its essence, identical with human influenza.

In their tenth paper the authors carry the matter farther by dealing in detail with the pathological findings in the respiratory infections caused by inoculation of *B. influenzae*. This part of the research is illustrated by eight plates of excellent photographs exhibiting the lesions. They emphasize the fact that influenza in man is almost never a fatal disease unless complicated by pneumonia, and on this account little opportunity has been offered of studying the changes of the pure influenzal disease, which appears to be a local infection of the upper respiratory tract with absorption of toxic products which cause the general symptoms. In experimental influenza in monkeys the pathological changes do not essentially differ from those that are met with in man. In both there is an acute catarrh extending from the nasal cavities into the trachea and bronchi. A bronchopneumonia is a frequent complication. The observations of morbid anatomists have shown that influenzal pneumonia possesses certain characteristic features, of which the most important are intense engorgement, haemorrhage, and oedema, with purulent bronchiolitis and scattered foci of peribronchial consolidation. Cecil and Blake describe these same changes in monkeys infected with cultures of *B. influenzae*, although in the latter it is usually a milder affection than in man. Attention is drawn to the fact that the pathogenesis of pure influenzal pneumonia is different from that induced by pneumococcus or streptococcus. In influenza, both natural and artificially produced, the infection seems to travel into the bronchioles, and subsequently involves the alveoli by contiguity, whereas in pneumococcus and streptococcus pneumonia the microbes quickly penetrate the bronchial mucous membrane and spread rapidly through the perivascular lymph spaces to the alveolar walls in all parts of the lobe.

All observations go to show that influenza bacilli possess but trivial invasive properties when compared to organisms like pneumococcus or streptococcus. The authors also note that in experimental infections by *B. influenzae* in monkeys there are changes in the thymus gland, including hyperplasia of the follicles, distension of the lymphatic channels, and infiltration of the parenchyma with leucocytes. These changes, however, are apparently part of a general hyperplasia of lymphoid tissues in the cervical and thoracic regions. The authors are to be congratulated on having greatly advanced knowledge on experimental pneumonia in their long series of researches, admirably conceived and carried out with great technical skill.

W. B.

**MAITLAND, H. B., COWAN, MARY L.,** and **DETWEILER, H. K. Spontaneous and artificial pulmonary lesions in guinea-pigs, rabbits, and mice.** *Brit. J. Exper. Path.*, 1921, **2**, 8.

A pulmonary lesion in guinea-pigs has been described which was characterized by haemorrhage into the alveoli and sometimes into the bronchioles. There was no leucocytic reaction in the lung-tissue, and no haemosiderin was present in the cells of the lung. This lesion is an agonal phenomenon. The same lesion occurred in rabbits and in mice, and is considered in them to be also an agonal phenomenon. Killing by rapid chloroform anaesthesia produced fewer agonal lesions than a blow on the back of the head. A method of killing has been described by which haemorrhage was not produced. A second type of lesion has been noted which is essentially a slow proliferation of endothelial cells. It is a spontaneous animal disease whose origin is undetermined. The haemorrhagic and proliferative lesion frequently occurred in the same area, but neither was dependent on the other. *B. bronchisepticus* was isolated from the lungs of sixteen guinea-pigs, but it was not possible to associate its presence with the proliferative lesion. P. F.

**STILLMAN, E. G.,** and **BOURN, JANET M. Biological study of the haemophilic bacilli.** *J. Exper. M.*, 1920, **32**, 665.

In 1919 Pritchett and Stillmann called attention to the existence of haemophilic bacilli almost indistinguishable from *B. influenzae* except by the fact that they can haemolyse blood. The present research is a further study of haemolytic bacilli, and includes a comparison of *B. influenzae* with haemolytic bacilli (now called Bacillus X) and with *B. pertussis*, *B. bronchisepticus*, and the bacillus of rabbit septicaemia. The haemophilic bacilli can be subdivided into two groups according to the ability of certain strains to produce haemolysin and consequent laking of blood. Both groups may be further subdivided according to the ability of some strains to produce indol, to form gas, and to ferment certain carbohydrates. The bacilli, of both groups, when grown in meat infusion bouillon containing 1 per cent. of dextrose, reach a final hydrogen-ion concentration of about $P_H$ 6·4. Almost all the strains can reduce nitrates to nitrites. The haemolysin of the lytic group is stated to be very stable, retaining its activity after being kept on ice up to several months. It can be demonstrated in a young broth culture only two hours old. It is non-filterable and is destroyed in half an hour at 56° C. The haemolytic, haemophilic bacilli are not pathogenic for guinea-pigs, rabbits, or mice. W. B.

**Bell, H. H. Relation of different strains of influenza bacilli as shown by cross-agglutination and absorption tests.** *J. Infect. Dis.*, 1920, **27**, 464.

In this investigation twenty-seven rabbits were immunized with as many strains of *B. influenzae*, five of which were obtained from normal persons, while twenty-two were recovered from cases of influenza. Each serum was then titrated with 36 cultures in dilutions varying from 1 : 25 to 1 : 6400. Absorption tests were also carried out. The author's results are presented in a series of tables from which it emerges that the influenza bacillus represents a heterologous group of micro-organisms as shown by agglutination and absorption tests. It was impossible by such methods to differentiate between influenza bacilli vegetating in the throats of normal persons and those isolated during the actual disease itself. A person may actually carry in the throat three different strains at one and the same time. W. B.

**Cooke, J. V. Complement fixation in influenza with *B. influenzae* antigens.** *J. Infect. Dis.*, 1920, **27**, 476.

This paper deals with complement-fixation tests in children and adults suffering from influenzal pneumonia. Although complement-fixing antibodies were obtained in the serum of a considerable number of older children and adults convalescent from the disease, they were found with much less constancy in children from 1 to 5 years of age. Further, no definite antigenic relationship could be detected between the sera tested and the 16 strains of influenza bacillus. W. B.

**Loewenhardt, F. E. R.** Zur Aetiologie der Influenza. [**On the aetiology of influenza.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, Orig. **85**, 81.

The author, who is assistant in the Hygienic Institute of the University of Breslau, under R. Pfeiffer, gives a lucid account of the epidemic of influenza as it affected Breslau in 1918, 1919, and 1920, and shows that the incidence of *B. influenzae* Pfeiffer showed a striking correspondence with the individual epidemic outbursts. In 187 cases of influenza, influenza bacilli were found in 65·62 per cent., viz. 57·14 per cent. in cadavera, 76·25 per cent. in sputum, and in 52 per cent. when the material was taken from the throat. When the material from the throat was examined at the actual bed-side, influenza bacilli were found in 91·11 per cent. of the cases. Material examined 4–6 hours later yielded a positive result in only 30·4 per cent. of the cases, whereas examined 24 hours later the results were completely negative as far as concerns *B. influenzae.* Of 397 non-influenzal cases only 35 (8·81 per cent.) showed influenza bacilli in the sputum, while of 101 throat examinations only 5 (4·95 per cent.) were positive, the percentage for the whole series of 498 non-influenzal cases being only 8·03. The author lays great weight on the bacteriological examination being carried out *immediately*, and on the use of pigeon's blood agar as the culture medium—Pfeiffer's original recommendation. W. B.

**Putnam, J. J.**, and **Gay, D. M.** **Behaviour of the influenza bacillus in mixed culture on haemoglobin-free media.** *J. Med. Research*, 1920, **42**, 1.

The authors attempted to grow *B. influenzae*, on a variety of blood-free media, in association with *B. xerosis*, *B. diphtheriae* (4 strains), *Diplococcus pneumoniae* (3 strains), *B. coli*, and two strains of a saprophytic staphylococcus. Sixteen cultures of *B. influenzae* were tested. The media employed were nutrient agar, with or without glucose, Martin's agar, glycerine egg medium. In the majority of instances the influenza bacillus failed to grow, and in fact the influenza inoculum died out. W. B.

**Fildes, P.** **The nature of the effect of blood-pigment upon the growth of *B. influenzae*.** *Brit. J. Exper. Path.*, 1921, **2**, 16.

(1) Growth of *B. influenzae* has not been observed to occur in the total absence of blood-pigment. (2) The quantity of blood-pigment necessary is small, but larger than has been stated. (3) Probably oxyhaemoglobin and carboxyhaemoglobin are incapable of allowing growth, the feeble multiplication in these pigments being due to a spontaneous change to methaemoglobin. Haematoporphyrin also fails to permit growth, but haematin allows a copious growth. (4) *B. influenzae* on suitable media grows fairly well under anaerobic conditions, but rapidly dies out. The necessary oxygen is obtained from an oxygen store in the medium. This store is not dissolved active oxygen, but is inactive in a state of loose combination with a constituent of the medium. Under aerobic conditions the combined oxygen is used up by the bacillus and immediately re-formed from the atmosphere. (5) The combined oxygen in the medium is activated for the bacillus by the catalytic action of iron in the pigment. (6) The feebleness of the growth on unchanged blood compared with that upon changed blood is due to a deviation of the oxygen, activated by the iron of the pigment, from the bacillus through the oxygen affinity of the unchanged pigment.
P. F.

**Olsen, O.** Ueber die Bedeutung des Blutes für das Wachstum des Pfeifferschen Influenzabazillus. [**The action of blood in the growth of the influenza bacillus.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, **85**, 12.

*B. influenzae* was found to grow equally well upon media containing pure crystallized horse haemoglobin and methaemoglobin as upon whole horse blood, in the familiar minute colonies. With pure haematin, however, growth was never obtained except in associated growth with other bacteria;

on the other hand, haematoporphyrin did not allow growth under any circumstances. Thus iron-containing pigment was necessary for growth.

From these experiments the author thought that independent growth of *B. influenzae* might depend upon the oxygen-carrying capacity of haemoglobin. He sought to show that the oxygen of haemoglobin might be utilized by the bacillus in its growth, by demonstrating a reduction of the pigment in the deeper layers of a 'deep' agar culture, such reduction being observed by him only in inoculated tubes. Such a function of haemoglobin was, however, obviously improbable in view of the equal growth with methaemoglobin, a pigment without oxygen-carrying capacity.

Next, the author observed that growth of the bacillus ran parallel to the catalytic action of the necessary pigment. Thus haemoglobin, methaemoglobin, and haematin were catalytic, but not haematoporphyrin. He concludes that the function of the pigment is probably to activate oxygen for the growth of the bacillus. P. F.

**Smith, J. D.**, and **Wilson, M. A. Comparison of smear, culture and complement fixation in chronic gonorrhoea in women.** *J. Immunol.*, 1920, **5**, 499.

This is a short paper based on 50 cases diagnosed clinically as mild chronic gonorrhoea, and 58 controls that were considered clinically not to be gonorrhoeal.

The antigen used was made from gonococci grown on disodium phosphate agar. These were treated with alcohol to remove lipoids, dried, weighed, powdered, and suspended in saline, 1 grm. to 200 c.c. This suspension was heated in a water-bath at 80° C. for 1 hour and then standardized. This antigen is said to be stable.

The culture tests were carried out on glycerine serum agar smeared with blood.

Of the 50 cases diagnosed clinically as mild chronic gonorrhoea only 7 were positive in film or culture; while 23 gave a positive complement fixation, 18 gave a weak positive and 9 were doubtful or negative.

The 58 controls were not examined by films or cultures and they all gave negative complement fixations.

It is concluded that a non-gonorrhoeic serum does not give a positive complement-fixation test, but a negative fixation test cannot exclude a chronic gonorrhoeic infection. The investigation, in part, was carried out in the Bureau of Laboratories of the Department of Health, City of New York. G. T. W.

**Thomsen, O.**, and **Vollmond, E.** Forsög paa Typeindeling af Gonococcer. [**An attempt to classify gonococci according to type.**] *Hosp.-Tid.*, 1920, **63**, 681–96.

Thomsen and Vollmond have attempted by agglutination and complement-fixation tests to distinguish various types of gonococcus. Their material consisted of 26 cultures of gonococci obtained from as many cases of recent urethritis in men. They soon found that complement fixation gave the most reliable and unequivocal results, and they noted that various cultures of gonococci were more or less easily agglutinated by the same quantity of agglutinin. By combining absorption with complement fixation, instead of relying on the combination of absorption plus agglutination, they were able to obtain the required information in a few hours, whereas 24 hours were necessary for the latter test, owing to the slowness of agglutination. With agglutination or complement fixation alone, they were unable to distinguish marked differences in the reaction of the various cultures to specific antisera. But when they combined these tests with that of absorption, they were able to classify the 26 cultures in 3 groups (types *a*, *b*, and *c*, including 14, 5, and 5 cultures each). The remaining 2 cultures could not be fitted into any of the above classes. Comparing their investigations with those of K. W. Jötten (vide *Medical Science*, 1921, **3**, 359), Thomsen and Vollmond note that this worker appears to have relied on agglutination and complement fixation only, and not to have employed the supplementary method of absorption. With regard to a possible relationship between the serological and clinical characteristics of their 3 types of gonococcus, Thomsen and Vollmond state that of the 14 cases belonging to type *a*, 5 were complicated by epididymitis and prostatitis, and the disease was protracted. Three cases were clinically slight, and 6 could not be traced. Of the 5 cases belonging to type *b*, 3 were very slight and 2 were very protracted. All of the 5 cases belonging to type *c* were slight and uncomplicated. C. L.

**FONTANA, A.**, e **SANGIORGI, G.** Sugli spironemi dei condilomi acuminati. [**On spironemata of pointed condylomata.**] *Pathologica*, 1920, **12**, 293.

Investigations were made in 20 different cases chosen among non-syphilitic subjects. The authors have been able to identify three forms of *Spironema*. The first one is termed by them Type A, and corresponds morphologically to the *Sp. refringens* of Schaudinn and Hofmann; the second is spoken of as Type B, and is similar to that found by Sangiorgi in 1916 in the human intestine; the third form is characterized by its similarity with the genus *Treponema*, and is very likely identical with the *Trep. calligyrum* described by Noguchi. C. d. F.

**SPIETHOFF, B.** Beitrag zu den Fehlerquellen bei der Salvarsanbehandlung. [**The sources of error in treatment by salvarsan.**] *Berl. klin. Wchnschr.*, 1921, **58**, 8.

In recent years there have been many records of untoward effects following the use of salvarsan. These include particular complications on the part of the liver, or of the nervous system. The present author was one of the early observers (1910) of salvarsan fatalities. In the communication now before us he reports the frequent occurrence of hepatic and nervous injuries. These made their appearance in an insidious manner from September 1913 onwards, and in the middle of 1914 actually 50 per cent. (!) showed jaundice. In this period he was using salvarsan dissolved in the patients' own serum, as experiments seemed to indicate that this combination was less toxic than watery solutions of the drug. At first jaundice was seen in those who had received a considerable number of salvarsan injections, later it occurred after a few. At one time there were no hepatic complications with watery solutions of salvarsan, but at the height of the 'epidemic' two cases of jaundice occurred even with these. Investigation showed that the same syringes were used both for the serum and for the watery salvarsan solutions. After use the syringes had been well washed in water, dried in air, and were kept in boxes with formalin tabloids. The replacement of these syringes by new ones is alleged to have been the cause of the cessation of the complications.

Neurotropic complications, such as symptoms of meningitis, lesions of a single cranial nerve, or severe psychoses, also made their appearance in groups of cases, and during courses of treatment which previously had been administered without detriment. These courses were in three stages: (1) a total of 6 grm. of salvarsan was injected (period of time not stated); (2) a 10 weeks' course of mercury in some form: (3) a last course in which a total of 3 to 4·5 grm. of salvarsan was given. Reference is made to 19 cases in which there were 'cerebral' complications. In 7, viz. 4 females and 3 males, the symptoms appeared in the second half of the first salvarsan series of doses. In 7 females the symptoms developed after the first dose of mercury, i. e. at the beginning of the second stage of treatment, while in 4 cases (3 females and 1 male) they appeared in the middle of the mercurial stage. Of the 19 cases, 15 were females and 4 were males. It is suggested by the author that in some mysterious way the complications were due to syringe 'errors', the instruments, in addition to salvarsan injections, having been used for injections of a calcium preparation called 'Afenil', the nature of which is not stated. The use of new syringes again caused a cessation of the cerebral complications. The cases of icterus were all mild and there was no instance of acute hepatic atrophy. The author discusses the possibility of the syphilis infection itself being partially accountable for the complications, but is unable to make any definite assertions. W. B.

**Ninni, C.** Sulla forma delle spore dei batteri del suolo. [**On the size of spores of the bacteria of the soil.**] *Pathologica*, 1920, **12**, 316.

If the earth of gardens or other soils be bacteriologically investigated, minute bodies are seen which have all the characteristics of ordinary spores with the exception of the size, which is only about half that of the ordinary ones. These small spores can be obtained artificially if sporogenous bacilli; for instance, *B. anthracoides* are cultivated by Pane's method on agar prepared with sterile water, and cultures kept for 24 hours at from 7° C. to 11° C. The author thinks that the small size of such spores is due to the relatively low temperature of the soil, because the same bacilli produce spores of the ordinary size if the cultures are left for another 24 hours at 31° C. This phenomenon cannot be in relation to nutritive conditions, because Pane has shown that *B. anthracis* produces spores of normal size if cultivated at 33° C. in distilled water. C. d. F.

**Capone, G.** Sulle variazioni della flora anaerobica in alcuni stati morbosi dell' intestino. [**Studies on the anaerobic flora in some morbid states of the intestine.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 54.

Systematic investigations on the morphological and cultural properties of the anaerobic flora of human intestine were carried out by the author, who for this purpose has examined samples of faeces of 12 healthy subjects, of 15 cases of bacteriologically ascertained forms of bacillary dysentery, of 4 cases of typhoid fever, and of 15 cases of enterocolitis. The cause of the latter could not be ascertained, as all investigations for protozoa, dysenteric or paratyphoid bacilli, and the like were attended with negative results, the aerobic flora of these cases appearing to consist chiefly of coliform bacilli.

The normal anaerobic flora appeared to be essentially formed by *B. perfringens*, which was found in almost all samples investigated. Moreover the following forms were identified: In two cases *B. sporogenes* of Metchnikoff (Strains P. 8–P. 11). In one case a bacillus similar to the variety B of *B. sporogenes* (P. 10). In another case *B. putrificus* of Bienstock (P. 16). In two cases, forms intermediate between *B. putrificus* and *B. para-putrificus* (P. 18–P. 19). Each of the following were seen once: *B. sporogenes non-liquefaciens* of Jungano (Bm. 25); a form similar to *V. septique* of Pasteur (Bm. 4); a strain similar to the bacillus of pseudo-oedema of Liborius-Sanfelice (Bm. 10); an unclassified anaerobic form (P. 22); and finally the *Clostridium foetidum* of Liborius-Sanfelice (P. 3).

The following strains were isolated from cases of dysentery; *B. perfringens*, frequently; a similar strain, once; strains similar to *B. III* of Rodella and *Species* IX of v. Hibler, four times; strains identical with *B. sporogenes non-liquefaciens* of Jungano, twice; a strain similar to *B. IV* of Rodella, once; strains similar to *V. septique* of Pasteur, thrice; a non-identified putrefying form, once.

The investigations made on samples from cases of enterocolitis were attended with similar results. The anaerobic flora of cases of typhoid fever was found to be chiefly formed by *B. perfringens* and putrefying forms; *Clostridium foetidum, B. sporogenes,* and a non-identified putrefying form were each found once.

From these results the author draws the conclusion that *B. perfringens* is constantly present in the human intestine and that the various circumstances which contribute to modify the flora of human intestine appear to have no influence on *B. perfringens*, but a considerable one on putrefying strains, which may in certain morbid states remarkably diminish in number and even completely disappear. C. d. F.

**Ninni, C.** Un nuovo bacillo anaerobico del suolo (*B. spermoide*). [**A new anaerobic bacillus of the soil (*B. spermoides*).** *Pathologica*, 1920, **12**, 385.

The new bacillus was isolated by the author from the soil of a high mountain (Mount Scagliolo), and is termed by him *B. spermoides* because of its morphological resemblance to the human spermatozoon. *B. spermoides* is pathogenic for the guinea-pig, in which it produces a form of chronic cachexia, but no tetanic symptoms of any kind. It is similar to *B. tetani*, but it can easily be distinguished from the latter because it is longer and larger, and because of various cultural characteristics, among which there is an acid formation, in any anaerobic medium, without the repugnant smell of *B. tetani*.[1] C. d. F.

**Heller, Hilda Hempl. Aetiology of acute gangrenous infections of animals: a discussion of blackleg, braxy, malignant edema, and whale septicemia.** *J. Infect. Dis.*, 1920, **27**, 385.

This is an important contribution to the difficult and involved question of acute gangrenous anaerobic infections in animals, especially cattle, horses, sheep, pigs. The authoress has manifestly made a most searching inquiry into the enormous and unsatisfying literature which has accumulated round these diseases, and she does not hesitate to pronounce most trenchant criticism where it is required. This renders her work all the more valuable in comparison with the numerous papers which are constantly pouring out with extensive bibliographies in which every observation by whomsoever made is treated with equal respect. Throughout her bibliographic studies are constant observations of her own, which clearly show that she speaks with authority. The confusion into which the bacteriology of anaerobes had fallen before the war was clearly stated by Weinberg and Séguin and was the principal cause which led the Medical Research Committee to institute a special committee of inquiry on anaerobic bacteria. This body aided materially in clearing up the confusion as far as concerns human pathogenic anaerobes. The present authoress has attempted something of the same kind with the even more uncertain and inadequately studied pathogenic anaerobes of animals. The paper, however, must be read in the original by workers on anaerobes, as it cannot be adequately dealt with here.

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[1] It may be pointed out that according to the Report of the Committee upon Anaerobic Bacteria (Medical Research Committee, Special Report Series, No. 39, 1919), p. 28, *pure* cultures of *B. tetani* have a characteristic but not a putrefactive odour.

W. B.

**House, S. John. Haemorrhagic meningo-encephalitis in anthrax: a report of three cases.** *J. Infect. Dis.*, 1920, **27**, 513.

The author gives a good description of three cases of cerebral complications occurring in anthrax. In two, the disease was not even suspected during life. The lesions were essentially extravascular, meningo-encephalitic, and the acute haemorrhagic non-purulent nature of the inflammatory exudate was like anthrax elsewhere. Large numbers of anthrax bacilli were found in the lesions. Two of the cases occurred in 'curled hair' workers who ultimately contracted intestinal anthrax, whereas the third—a boy of 15—seemed to have had no direct connexion with anthrax-infected products. A clinical diagnosis was not made, but mastoid abscess with lateral sinus thrombosis was suspected. The cerebral infection was believed to have been by the haematogenous rather than by the lymphogenous route.

W. B.

**Fukuda, A.** Experimentelle Untersuchungen über Milzbrandinfektion bei Ratten. [**Experiments on anthrax infection in rats.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, Orig. **84**, 516.

In the last decade of last century, a great deal of labour was expended on the study of the action of anthrax bacilli on the highly immune rat, and many experiments were undertaken to investigate the methods by which the natural immunity could be broken down, and the animal rendered susceptible to anthrax. The present author, working in the Hygenic Institute in Zurich, has again made a study of this question, and especially the influence of calcium chloride, which was shown by Bullock and Cramer to increase the liability to tetanus and other anaerobic bacteria. Instead of rendering rats more susceptible to anthrax, his experiments go to show that, in quantities of 0·001 to 0·03 grm., calcium chloride injected simultaneously with anthrax culture retards, as a rule, the course of the disease. He also finds that anthrax bacilli injected into rats already infected with nagana trypanosomes, has a delayed effect. There was also an apparent

antagonism between *B. anthracis* and *B. pyocyaneus*—an old view revived. Starting with a culture which was only slightly pathogenic for the rat, the author, by means of 12 rat passages, raised the virulence so that $\frac{1}{3}$ of a loopful of a culture on agar killed rats constantly in 27 to 54 hours. It was with such virulent cultures that the above experiments were carried out.
W. B.

**Lubinski, H.** (1). Bakteriologisches zur Frage der Wunddiphtherie. [**Bacteriology of wound diphtheria.**] *Berl. klin. Wchnschr.*, 1920, **57**, 1154.

**Lubinski, H.** (2). Bakteriologische Untersuchungen über Wunddiphtherie. [**Bacteriological researches on diphtheria of wounds.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, Orig. **85**, 96.

These two papers deal with one and the same material, the first being an abridgement of the second. The bacteriological examination of wounds revealed in a number of instances the existence of bacilli, presenting close resemblance with *B. diphtheriae*. A closer investigation showed, however, that only a certain number were genuine diphtheria bacilli, a considerable proportion differing in the fact that they were able to ferment saccharose and that they were non-pathogenic. The author calls this organism paradiphtheria bacillus. Of 105 samples from wounds, 18 showed true diphtheria bacilli, and 46 were of the saccharose-fermenting paradiphtheria type. Of the true diphtheria bacilli found, 10 were found to be non-toxic. The author regards paradiphtheria as harmless for animals and quotes an experiment in which the same is probably true for man. A quantity of 0·05 c.c. of a paradiphtheria strain grown 10 days in bouillon was injected intracutaneously into a human being without result. In future examinations of diphtheria in wounds he emphasizes the necessity of testing not only the toxicity but also the fermentation results on a number of carbohydrates, particularly saccharose.
W. B.

**Grönberg, J.** Studier öfver blodfermenten vid graviditet, karcinom och lungetuberkulos. [**Studies of the blood ferment in pregnancy, carcinoma and pulmonary tuberculosis.**] *Finska Läk-sällsk. Handl.*, 1920, **62**, 599–631.

Grönberg, whose investigations were made under Abderhalden in Halle, and Granberg in Viborg, classifies the literature of Abderhalden's test according as the authors obtained good or bad results. The bibliography for the first class occupies a page and a half, for the second a little more than half a page. Much of his paper deals with technique, and he reiterates the warning that, without meticulous care in every detail, the test is of little value. He has tested collodium dialysers and found them unsatisfactory. To ensure objectivity of judgement, he kept himself in ignorance of the clinical diagnosis of the cases from which sera were obtained. In all the 28 cases of normal pregnancy between the 1st and 9th month, a positive reaction was obtained with placental tissue, whereas all the 19 control sera from healthy, non-pregnant individuals gave a negative reaction to placental tissue. All the sera of 23 patients suffering from carcinoma in various stages gave a positive reaction to a substrate obtained from carcinomatous liver with metastases. All the control sera of healthy persons gave a negative reaction to the same substrate. All the sera of 34 cases of pulmonary tuberculosis gave a positive reaction to a substrate obtained from tuberculous lungs. Of these 34 cases, 8 were in Turban's first stage. and 11 were in a still earlier stage, being merely suspects. Grönberg evidently considers that Abderhalden's test requires so great technical skill that its practical utility is much limited. C. L.

**Becker, G.** Om komplementbinding hos botriocefalusbärare. [**Complement fixation by the hosts of *Bothriocephalus*.**] *Finska Läk-sällsk. Handl.*, 1920, **62**, 632–47.

Becker's answer to the question: Does *Bothriocephalus* give rise to antibodies in the serum of its host? is reserved. Probably it does so, but the reaction is almost certainly not specific. He examined 58 persons harbouring *Bothriocephalus* and 92 in whose faeces there were no signs of it. He classifies the reactions according as there was no haemolysis, slight, almost complete, or complete haemolysis. Including slight haemolysis among the positive reactions, he found these in about 50 per cent. of the *Bothriocephalus* carriers and in only about one-ninth of the healthy controls. Some of these, he adds, may have harboured the *Bothriocephalus* in spite of the examination being negative. Positive reactions were obtained when a *Taenia* antigen was tested with the serum of a *Bothriocephalus* carrier, and when a *Bothriocephalus* antigen was tested with the serum of a *Taenia* carrier. Hence Becker's doubts as to the specificity of the reaction. C. L.

**Ficai, G.** Osservazioni sierologiche sul tifo esantematico. [**Serological studies on typhus.**] *Ann. d'ig.*, 1920, **30**, 395.

The agglutinins for *Micrococcus melitensis* do not appear earlier in the blood than those for *B. proteus* X 19, and very soon disappear. The Wassermann reaction is in most cases at first negative, but becomes positive in the course of the disease and then negative again. The Wassermann reaction has, therefore, no diagnostic value, but it may be useful in showing the existence of profound modifications in the blood of typhus patients. The diagnostic value of the Weil reaction is almost absolute; but the practical value is in strict relation to the sensitiveness of the strain of *B. proteus* X 19 used. In practice it is useful to have at hand strains of *B. proteus* X 19 of different origin, as some strains appear to have various degrees of sensitivity when tested with the serum of patients coming from different places. The studies of recent years prove that the virus of typhus causes an intense reaction on the part of the organism during which agglutinins, produced during other infections already overcome, are brought into action again. C. d. F.

**Schütze, H. Haemagglutination and its medico-legal bearing, with observations upon the theory of isoagglutinins.** *Brit. J. Exper. Path.*, 1921, **2**, 26.

The possibility of grouping dried human blood specimens by reconstructing the serum for agglutination and using the undissolved residue for absorption has been demonstrated. Forensically, the test would be of most importance when proving dissimilarity between two specimens alleged to be derived from the same source. To prove their similarity would probably only be to furnish circumstantial evidence of more or less value according to the group in question and the frequency of the occurrence of that group in the population concerned. The Landsteiner theory that two substances, 'A' and 'B', with their corresponding agglutinins, 'a' and 'b', are concerned in the isoagglutination of human bloods has been confirmed by absorption tests. P. F.

**Kodama, R. Ocular reactions in anaphylaxis.** *J. Infect. Dis.*, 1921, **28**, 48.

This is an interesting study of the anaphylactic effects on the eyes of guinea-pigs sensitized with horse serum. Preliminary observations and measurements were made on the width of the lids and the pupil, the iris being examined by a magnifying lens under electric light. Measurements are given showing the effect of instilling saline solution or normal horse serum into the eyes of normal guinea-pigs, of normal horse serum, heated or unheated, into the eyes of sensitized guinea-pigs, the injection of normal horse serum into the orbits of normal and sensitized guinea-pigs, intravenous injections of serum in normal and sensitized guinea-pigs, and other variations. Generally speaking, the application of normal horse serum to the eyes of normal or sensitized guinea-pigs produces dilatation of the lids and pupils succeeded by contraction. In the sensitized animal the response is more prompt and vigorous. The primary dilatation appears to be the result of stimulation of the tarsal smooth muscles of the lid and the dilator smooth muscle of the iris. The secondary narrowing of the lid fissure may be explained as due to the loss of tone of the tarsal muscle and dilator pupillae on one hand, and to the contraction of the sphincter of the iris associated with congestion on the other hand. The primary and secondary effects on the smooth muscles of the lid and iris suggest that the anaphylactic action involves the ends of both the true and parasympathetic nerve-fibres on both sets of plain muscles in the lid and the iris.

Anaphylactic intoxication with horse serum may also be associated with circulatory disturbances, such as oedema and congestion of the lid, conjunctiva, iris, and fundus. The direct application to the eye of horse serum, heated or unheated, may cause vascular dilatation in the normal, but haemorrhage is observed especially in the sensitized animals. As it takes place independently of asphyxia it is due to direct action on the vessels. In addition to the characteristic post-mortem appearances of anaphylactic shock there is a rapid and strong contraction of the pupil after anaphylactic death. As all the anaphylactic eye phenomena appear to be an intensification of the reaction that follows the application of horse serum to the eye of the normal guinea-pig the author suggests that the normal animal possesses small quantities of the anti-substances necessary for the anaphylactic reaction. W. B.

**Howell, Katherine M., and Eby, Harriet. The transmission of specific immune bodies from the mother to the young.** *J. Infect. Dis.*, 1920, **27**, 550.

The authors carried out a number of experiments to determine: (1) the effects of parturition on the antibody content of immunized rabbits; (2) the antibody content of the serum of the offspring of immunized rabbits; and (3) the durability of the immune bodies in the serum of the offspring of immunized mothers. Six rabbits were employed, one being immunized against human, the second against sheep's erythrocytes, the third against

*Streptococcus viridans*, the fourth against *Diplococcus pneumoniae* (Type II), the fifth against *Micrococcus meningitidis*, and the sixth against *B. typhosus*. A high degree of immunity was maintained by a weekly dose of the immunizing agent *during* pregnancy, but this was discontinued after pregnancy. The blood of mothers and offspring was tested as soon after parturition as possible. In the sera of the mothers antihuman and antisheep lysins diminished after parturition. The sera of the offspring of immunized mothers exhibited haemolysins, but in lesser amounts than that of the mothers. In the young the lysins disappeared completely within eleven weeks. For the most part the complement-fixing antibodies, opsonins, and agglutinins showed a like course. W. B.

**Browning, C. H., and Wilson, G. Haswell. The antigenic properties of globin with a note on the independence of the properties of serum and tissue proteins as exemplified by the absence of antibody from the globin of an immunized animal.** *J. Immunol.*, 1920, **5**, 417.

By means of Schulz's method the authors prepared solutions of globin from the haemoglobin of guinea-pigs and some other animals, and by injection into rabbits claim to have produced antisera which can be demonstrated by complement-fixation methods. Apparently, success is obtained only in the case of certain individual animals, and this may explain the negative results obtained by Schmidt, and by Gay and Robertson. Positive complement-fixation results depend on suitable quantitative relationships between antigen and antibody, as also upon a suitable hydrogen-ion concentration. The reactions with the antisera show in certain cases that there is a marked species-specificity, for if one reckon the amount of complement fixed by guinea-pig globin in the presence of the homologous serum as 100 per cent., rabbit globin fixed 16 per cent. of complement, and ox globin less than 6 per cent. On the other hand, anti-ox globin, fixes complement in the presence of goat, duck, and guinea-pig globin, but not when rabbit globin is the antigen used. The authors believe that the antibody is a genuine antiglobin and is not due to any adventitious protein contamination during the preparation of the globin antigen. In a note they describe the result of an experiment in which a rabbit was immunized with red corpuscles of the ox until its serum was powerfully haemolytic. Blood having been drawn from this immunized rabbit, an extract of its globin was prepared, but although used in strong concentration produced no haemolysis of ox corpuscles. W. B.

**Matsumoto, Motomatsu. Experiments upon the production of antihuman haemolysin with special reference to immunization with erythrocytes sensitized with heated serum.** *J. Immunol.*, 1920, **5**, 507.

The difficulty of producing high grade antihuman haemolytic sera by the immunization of rabbits with human red blood corpuscles is known to all immunizators. The injurious effects of the inoculations have been ascribed to anaphylaxis, direct toxicity of the antigen, or to fatal embolism due to agglutination of the red cells introduced. The most recent work tends to eliminate the view that the phenomena are anaphylactic. The present author confirms the statement of Vedder that exposure of human erythrocytes to antihuman serum, diluted 1 : 10 and heated to 70°–80° C., reduces the susceptibility to haemagglutinin formation which otherwise may cause injury or death of the animal. Solutions of human erythrocytes in distilled water and largely freed of shadow corpuscles are much less toxic and are better tolerated than suspensions of whole cells, and although the yield of haemolysin may be slightly less are to be preferred as antigens.

W. B.

**Pardi, U.** Sopra l'azione di sieri concentrati. [**On the action of concentrated sera.**] *Pathologica*, 1912, **12**, 388.

Concentrated serum of guinea-pigs is, within certain limits, innocuous if injected intravenously in other animals of the same species; but it is fatal, even in small doses, if injected subdurally. Concentrated serum of dog has the same effect if injected subdurally into guinea-pigs. This fatal action of the subdural injections is attributed by the author to the concentration of the colloids of the serum, these probably having a direct influence on important nerve centres. C. d. F.

**Ponticaccia, L.** Ricerche sperimentali sull'azione emolitica ed anemizzante dell'acido oleico e delle trioleine nei conigli. [**Experimental investigations on the haemolytic action of oleic acid and trioleins in rabbits.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 35.

Oleic acid has a remarkable haemolytic action *in vitro,* as well as *in vivo,* this, however, being very much checked by the reaction of the healthy organism if, of course, the acid is not put in direct contact with the circulating blood. The reaction of the organism consists, first of all, in a local inflammatory process by means of which the injected mass becomes circumscribed from the surrounding tissues and only little of it can pass very slowly into the blood-stream. There is, in the second place, a formation of more resistant erythrocytes as can be proved by testing them with hypotonic solutions of NaCl. Lastly, there is a production of specific antihaemolysins, these having very likely an extrasplenic origin. Rabbits treated with subcutaneous injections of oleic acid show only a form of simple anaemia which *per se* is not fatal and has none of the characteristics of the progressive pernicious form. The lesions caused in the digestive organs by the same treatment are also very slight and not at all similar to those seen in progressive pernicious anaemia.

Ordinary oils (trioleins of olive, cotton, and linseed) may cause a very slight anaemia in rabbits if administered *per os* in large quantities and for a long time. This slight anaemia appears to be due, not to a possible haemolytic action of the oleic acid freed from its glycerol, but to digestive troubles, and to a diminished absorption of nourishing materials caused by the great mass of oil occupying the enteric tube. By the administration of varying doses of oils it has been impossible to cause in rabbits any change similar to those of the progressive pernicious anaemia. The anatomical lesions observed are simply those to be expected after the forced and repeated introduction into the gastro-enteric tube of large quantities of fats.

C. d. F.

**Hill, L.**, and **McQueen, J. M.** **The measurement of capillary blood-pressure in man.** *Brit. J. Exper. Path.*, 1921, **2**, 1.

That pressure which stops the flow through and expresses blood from the skin has been generally taken as signifying the capillary blood-pressure.

In truth it indicates the pressure in the small arteries which feed the compressed part after an allowance has been made for error arising from the pressure required to deform the convex horny layer of the skin. The method devised measures this error and arrives at the true pressure in the small arteries. The pressure of a small jet of water is found which will just blanch the skin of the hand held at heart level (1) in the normal condition, and (2) with the capillaries at zero pressure after the veins of the forearm have been emptied by gravity and the brachial artery occluded by a tourniquet. When (2) is deducted from (1) a reading of about 10 mm. Hg is obtained. Reference is made to previous measurements of capillary pressure in the brain, &c., and to recent experiments carried out on transparent membranes of frogs, mice, &c., by one of the authors (L. H.). These show that a momentary compression equal to 2–5 cm. water suffices momentarily to check the flow of corpuscles in the arterioles or their main capillary branches. The true capillary pressure as indicated by these figures is a very low one, and theories of lymph-formation, &c., based on a capillary pressure of some 30 mm. Hg must be modified accordingly. The relation of the swelling of the tissue-cells to the capillary circulation in inflammation is discussed, also the relation of the pressure of the cerebrospinal fluid, aqueous humour, and salivary secretion. P. F.

**Azzi, A.** Sul parallelismo fra reazioni vaso-motorie periferiche e polmonari. [**Parallelism between peripheral and pulmonary vasomotor reactions.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 25.

Reference has already been made to the strict relations existing between cutaneous and pulmonary vasomotor conditions (see Viale, G., *Medical Science*, 1921, **3**, 371). Azzi's investigations are much on the same lines with this difference, that he has made use of emotional and thermal stimuli to cause peripheral vasomotor changes. These were registered by means of Mosso's plethismograph, while the temperature of the expired air was measured by means of a thermo-electric cell. The results obtained can be summarized thus: There is a constant diminution in the temperature of the expired air for every peripheral vasoconstriction, however caused.

C. d. F.

**Novaro, P.** Ricerche calorimetriche comparative sul digiuno e sull' avitaminosi. Nota III. [**Calorimetric investigations on inanition and deficiency disease. Note III.**] *Pathologica*, 1920, **12**, 183.

Reference has already been made to the investigations of this author (*Medical Science*, 1921, **3**, 372). She has now published an additional note, in which the period of convalescence both from starvation and deficiency disease are comparatively examined. The conclusions arrived at are: (1) The temperature of the convalescent pigeons returns to 41° C. during the first 24 hours, independently of the minimum reached during inanition or deficiency disease. Four or five days are then necessary for the body temperature to reach the normal average of 42° C. (2) The amount of heat given off, though greater than that of the last day of starvation or deficiency disease, remains, in proportion to the body-surface, below the normal average as long as the temperature has not become normal. Afterwards, it becomes greater than the normal average as long as the body-weight has not also become normal. (3) With the exception of the first day of convalescence the animals take a quantity of food the energy value of which may be even 50 per cent. above the normal average. This continues until the body-weight becomes about the same as at the beginning of the experiments. (4) The body-weight increases very rapidly in the first two days of convalescence, the further increase being more gradual and rather slow. However, the increase in body-weight is not always regular, but may show various oscillations. (5) A strict relation appears to exist between the various metabolic factors and variations in the body-weight. (6) All other conditions being the same, the period of recovery lasts longer after deficiency disease than after inanition. C. d. F.

**Novaro, P.** Sulle modificazioni del tessuto interstiziale in seguito a deficienza di vitamina B nella dieta. [**Changes in the interstitial tissue of the testicle in consequence of deficiency in water-soluble accessory substance B.**] *Boll. d. Accad. med. di Genova*, 1920. (*Pathologica*, 1920, **12**, 405.)

The testicles of four young pigeons, kept for two months on a diet of polished rice, were examined histologically. Material was fixed partly in Zenker and partly in Flemming. The testicular tubules were found atrophic, and their epithelium degenerated in many places. The intertubular spaces were larger than in normal specimens and filled with interstitial cells. These, instead of appearing isolated or in small groups of two or three, were arranged in well delimited rows supported by flattened connective tissue elements. The interstitial cells had increased, not only in number, but also in size, their nuclei being also larger than those of normal cells. In the specimens fixed in Flemming's fluid the cytoplasm of such cells appeared filled with many granules stained deeply black. The author comes to the conclusion that deficiency of the water-soluble accessory food factor B, causes a true hypertrophy and hyperplasia of the so-called interstitial gland of the testicle. C. d. F.

**De Albertis, D.** Su di un metodo rapido per la colorazione della nevroglia fibrillare. [**Quick process for staining neuroglia fibres.**] *Pathologica*, 1920, **12**, 240.

The process results from an original combination of the methods of Weigert, Mallory, and L'hérmitte, and is meant to be chiefly used for ascertaining quickly the possible existence of a proliferation of neuroglia fibres in pathological specimens.

Sections are made by means of a freezing microtome from pieces fixed in 15–20 per cent. formalin for about 24 hours, but no longer than three days. They are collected in distilled water, transferred into a bath of 2 per cent. acetic acid in 1 per cent. chromic acid (time not stated), washed for some hours in repeatedly changed distilled water, oxidized for 10–15 minutes in half per cent. potassium permanganate, washed again in distilled water, reduced for 15–20 minutes in 1 per cent. oxalic acid, and, lastly, put to stain for 12–24 hours in a saturated solution of Victoria blue. For the further treatment, sections are washed in distilled water and from this lifted, one by one, by means of a thin glass or platinum spatula, this to be also used to plunge each section, for an instant, first into concentrated Lugol's solution, then into absolute alcohol, and, lastly, into equal parts of xylol and aniline oil, where the differentiation is accomplished in a few seconds. Sections are finally collected and washed in slightly warmed and repeatedly changed xylol, and mounted in xylol-dammar without a cover. Neuroglia fibres are deep blue and red-blood corpuscles pale blue on an unstained background. C. d. F.

**Zappa, P.** Contributo di osservazioni alla determinazione della formula leucocitaria normale. [**On the normal leucocytic formula.**] *Pathologica*, 1920, **12**, 296.

In 1914 A. v. Bonsdorff (*Finska läk-sällsk. handl., Helsingfors*, 1914, **2**, 1471), tried to show that if blood is regularly examined in the early hours of the morning and before breakfast, the number of mononuclear leucocytes is found to be almost the same as that of neutrophil polymorphonuclear leucocytes, while the normal proportion established by Ehrlich and Einhorn, and almost universally accepted as right, is of about 25 to 75. The author of the present paper has taken advantage of a systematic series of examinations carried out, during 1917, 1918, and 1919, on young and healthy subjects (soldiers) with the object of controlling v. Bonsdorff's data, and of seeing how far he was possibly right. It thus resulted that the normal number of mononuclears in proportion to the polynuclears in the leucocytic formula should be considered higher than is generally believed. The proportion between the former and the latter can be expressed by the fraction $\frac{39}{61}$, which is very near to the fractions $\frac{38}{62}$, $\frac{39}{61}$, $\frac{39{\cdot}5}{60{\cdot}5}$, $\frac{41{\cdot}9}{58{\cdot}1}$, $\frac{42}{58}$ representing the values obtained by Jolly, Ostenfeld, Galambos, Türk (1912), Mehrthens, and Bunting. All these values are higher than those given by Einhorn $\frac{25}{75}$. Ehrlich and Lazarus $\frac{26}{74}$, Türk (1904) $\frac{26{\cdot}9}{73{\cdot}1}$, v. Torday $\frac{31{\cdot}7}{68{\cdot}9}$, Leredde, and Besancon $\frac{32{\cdot}5}{67{\cdot}5}$, but still remarkably smaller than the fractions $\frac{50{\cdot}4}{49{\cdot}6}$ and $\frac{52}{48}$ of v. Bonsdorff. C. d. F.

**Giuliani, R.** Neutralizzazione sessuale ottenuta mediante sieri orchilitici ed ovariolitici. [**Sexual neutralization obtained by means of orchilytic and ovariolytic sera.**] *Ann. d'ig.*, 1920, **30**, 323.

Preliminary note on experiments made in rabbits by means of an orchilytic serum obtained by injecting nucleoproteid from rabbit's testis into a sheep. The results, though very incomplete, are worth mentioning as they show that it is perhaps possible to cause a total atrophy either of the testes or of the ovaries by means of properly prepared sera—a problem of great interest both from scientific and practical points of view. C. d. F.

**Pistocchi, G.** L' influenza della milza, del rene, della tiroide nella produzione della crisi anafilattica. [**On the influence of the spleen, kidney, and thyroid on the anaphylactic shock.**] *Pathologica*, 1920, **12**, 239.

Experiments were carried out on guinea-pigs, which had undergone sensitization a few days after extirpation either of the spleen or of one kidney or of the thyroid. Splenectomy and nephrectomy had no influence on the production of the anaphylactic shock; thyroidectomy prevented the latter in most of the animals on which the experiment had been performed.

C. d. F.

**Rusca, C. L.** Sul morbo di Gaucher. [**On Gaucher's disease.**] *Atti d. Soc. lomb. sc. med. e biol.*, 1920, **9**, 354.

Preliminary communication on exhaustive histopathological investigations carried out on the spleen, lymph glands, bone-marrow, thymus, and solitary follicles of the intestine of a typical case of Gaucher's disease observed in a baby of only eleven months. The characteristic Gaucher cell was found in all organs examined, and the author consequently thinks that the disease ought to be considered as affecting the whole haemo-lymphopoietic system, the splenomegaly being only the chief clinical symptom.

C. d. F.

**Sampietro, G.** Osservazioni sierodiagnostiche nel tifo petecchiale. [**Serodiagnostic studies on typhus.**] *Ann. d'ig.*, 1920, **30**, 593.

A series of careful investigations summarized by the author as follows: (1) The Weil-Felix reaction was positive in 5·5 per cent. of the normal sera examined, but with dilutions smaller than 1 : 100. It was also positive in 18 per cent. of the investigated sera of typhoid fever patients, but with dilutions sometimes smaller, sometimes larger than 1 : 100. The reaction was negative in cases of small-pox and other eruptive diseases. (2) In the sera of cases of small-pox, agglutinins for *B. typhosus* may temporarily appear. (3) The Weil-Felix reaction is positive in practically all cases of typhus, but only from the end of the first week, if investigations are carried out with dilutions not smaller than 1 : 100. (4) Agglutination curves for Proteus X 19 may be of three different types according to the length of time during which agglutinins remain in the blood. This permanence is, in its turn, in direct relation to the degree of concentration reached by the agglutinins themselves in the patients' blood. They generally persist for about two months, but were found even after four. (5) The agglutination curve may show a sudden but quite temporary fall, particularly at the beginning or towards the end of the curve. (6) The serum of typhus patients agglutinates *B. typhosus* in 87 per cent. of the patients vaccinated against it, and in 21 per cent. of the non-vaccinated patients. Widal's reaction may therefore be independent from antityphoid vaccination in typhus patients, but the latter influences the results, increasing the percentage of positive cases. (7) If both Widal and Weil-Felix reactions are positive, a serological discrimination between typhoid fever and typhus can be attained only by following the agglutination curves of both forms. (8) 63 per cent. of the sera showing a positive Weil-Felix reaction also agglutinate a serological type of *B. pyocyaneus* in dilutions even greater than those required to agglutinate the Proteus X 19. As in the case of Proteus there are species of *B. pyocyaneus* which do not agglutinate. (9) As shown by Castellani's test the agglutinins for *B. pyocyaneus* are independent of those for Proteus X 19. By the same test the agglutinins for *B. typhosus* appear sometimes as co-agglutinins, sometimes as independent agglutinins. (10) The poly-agglutination of the serum of typhus patients is probably due to the mobilization of specific latent agglutinins produced during other, already overcome, infections. (11) The Weltmann reaction is neither specific nor constant; however, it may be useful for laboratory work. (12) The Wassermann reaction, made with sera of typhus patients, has been attended by negative results. C. d. F.

**Nagao, K. The. fate of india ink injected into the blood. I. General observations.** *J. Infect. Dis.*, 1920, **27**, 527.

The author has made a careful examination of the tissues of rabbits and guinea-pigs which had been injected intravenously with a suspension of very fine particles of indian ink. For this purpose a stick of indian ink was rubbed on an ink stone with a small quantity of 0·8 per cent. salt solution. The suspension was then centrifugalized, and the upper part was filtered several times through paper, the resulting fine suspension being then sterilized discontinuously by steam. As a rule about 0·4 c.c. per kilo was the amount injected. After injection the mucous membranes and spleen became black, and this condition persists for some time. Ink granules are deposited regularly in the endothelial cells of the liver, spleen, and marrow, and in the splenocytes. Only a small number of granules were found in the adrenals, kidneys, or lungs. In the spleen the granules were irregularly accumulated at the periphery of or actually in the Malpighian corpuscles. Granules were not found in the parenchyma cells of the nervous system. In the blood, polymorphonuclear neutrophilic, and mononuclear cells, were found to have taken up granules, but large lymphocytes did so only rarely. Eosinophils and mast cells were not found with granules. Apparently, ink granules were not discharged from the body by any particular organ.

W. B.

**Parrino, G.** Ricerche sperimentali sulla fagocitosi. Sulla influenza che spiegano sulla fagocitosi vari fissatori del protoplasma batterico. [**Experimental investigations on phagocytosis. Influence of various fixing agents.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 76.

**Di Macco, G.** Ricerche sperimentali sulla fagocitosi. Modificazioni della fagocitosi per effetto della fatica. [**Experimental investigations on phagocytosis. Influence of fatigue.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 81.

**Calderone, A.** Ricerche sperimentali sulla fagocitosi. Modificazioni della fagocitosi per l'azione di soluzioni diluite di acido cloridrico. [**Experimental investigation on phagocytosis. Influence of diluted solutions of hydrochloric acid.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 274.

These three papers form part of a series of systematic investigations on phagocytosis, carried out under the direction of V. Scaffidi at the Institute of General Pathology of the University of Palermo.

Parrino has studied the influence on phagocytosis of various fixing agents such as alcohol, formalin, corrosive sublimate, chromic acid, and osmic acid. Investigations were carried out by a very exact method and carefully controlled, Eberth's bacilli being used as test. It was found, that while alcohol, formalin, and corrosive sublimate render Eberth's bacilli more resistant to the phagocytic power of polymorphonuclear leucocytes, both chromic and osmic acids have the opposite effect with a corresponding increase in the so-called phagocytic value. It is interesting to note that this effect can be also obtained by means of corrosive sublimate if this is re-dissolved after fixation by treating the bacilli with Lugol's solution. This appears to indicate that the obstacle to phagocytosis is not always due to the protoplasmic modifications caused by the fixing agents, but to the combinations which these last form with the protein of the bacteria used as tests.

Di Macco has studied the modifications in the phagocytic power of polymorphonuclear leucocytes in guinea-pigs in the last stages of exhaustion, a state brought about by means of a very simple apparatus which compelled them to run at a known speed. The phagocytic index or value was determined for every animal before and after each experiment by the same method and tests as used by Parrino. Di Macco comes to the conclusion that acute fatigue causes a diminution of the phagocytic index, this being reduced to about 25 per cent. of the normal value. This result agrees with that arrived at by Ferranini and Fichera by means of a quite different method. The diminution in the phagocytic index appears to be a direct consequence of the influence of fatigue poisons on the various elements of the blood. Three or four days are necessary for the phagocytic index to again become normal, this fact pointing to the general conclusion that fatigue poisons are only slowly destroyed or eliminated.

Calderone has investigated the influence of diluted solutions of hydrochloric acid made to act for various periods of time on Erberth's bacilli used as test. Experiments were attended by unexpected results in that it clearly appeared that the phagocytic value diminished when bacteria were kept in contact with dilutions of HCl N/50–N/100 for some hours up to 24, but it gradually increased when the contact was further prolonged. On the contrary, when working with more diluted solutions as, for instance, N/800–N/1,000, the opposite phenomenon was noticed, the phagocytic index showing an increase in the first two hours and a diminution in the subsequent periods of time. The diminution of the phagocytic index in the first hours of contact of bacteria with little diluted solutions of HCl can be explained, assuming that the chloro-protein which becomes thus formed has a negative chemotactic power on polymorphonuclear leucocytes. The subsequent increase under the same experimental conditions is very likely due to deep changes in the bacterial protoplasm owing to the prolonged influence of the HCl. As a matter of fact, there is a certain coincidence of time between the increase of the phagocytic index and the death of the bacteria experimented upon. But the transitory increase of the phagocytic index at the beginning of experiments made with very diluted solutions of HCl remains entirely inexplicable. The author can only point out that a similar fact was observed by Oker-Blom (*Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1912, Orig. **14**, 485) when treating staphylococci with N/1,000–N/2,000 dilutions of sulphuric acid.

In conclusion, phagocytosis is influenced not only by the biological activity of bacteria but also by changes caused in them by the substances with which they come in contact and by the length of time during which this contact is prolonged. C. d. F.

# BIOCHEMISTRY

**Peters, J. P. (Jr.), and Barr, D. P. The carbon dioxide dissociation curve and the arterial and venous carbon dioxide tension of human blood in health and in disease.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **18**, 5.

A method for the direct determination of the carbon dioxide tension of human arterial and venous blood has been applied to the examination of 23 subjects on whom 38 observations have been made. The method is similar to that of Means, Bock, and Woodwell (*Trans. Am. Assoc. Physicians*, 1920). The group consisted of 3 normal persons, 6 with severe anaemia, 4 with diabetes, 2 with emphysema, 1 with polycythaemia, and 1 with chronic nephritis. The alveolar carbon dioxide tension was also determined in some cases.

In three cases of cardiac decompensation the dissociation curves lay below the normal limits indicating a real reduction in available alkali. The carbon dioxide capacity of the venous plasma was normal. In these cases, therefore, the latter method is inapplicable as a measure of the available alkali of the blood.

The dissociation curve in severe anaemia is more nearly horizontal, and lies at a higher level than does the normal dissociation curve at carbon dioxide tensions that exist in the body. This is due to the diminution in haemoglobin which has the power of combining with a part of the alkali of the blood. In cardiac dyspnoea the difference between alveolar and arterial $CO_2$ tension was always much greater than normal, varying from 13–19 mm. Hg. This indicates some impairment of the mechanism for the elimination of carbon dioxide from the lungs. C. G. L. W.

**Hendrix, B. M., and Crouter, C. Y. Relation of the alkali reserve of the blood to glycosuria and hyperglycaemia in pancreatic diabetes.** *J. Biol. Chem.*, 1920, **45**, 51.

The results are against Murlin and Sweet's view of the causal relation between the acid of the gastric juice and pancreatic diabetes. In dogs from whom the pancreas had been removed the decrease in alkali reserve of the blood appeared considerably later than the hyperglycaemia and glycosuria, thereby indicating that it was not a neutralizing function of the pancreas that was at fault. R. A. P.

**Palmer, W. W., Salvesen, H., and Jackson, H. Relationship between the plasma bicarbonate and urinary acidity following the administration of sodium bicarbonate.** *J. Biol. Chem.*, 1920, **45**, 101.

By the method of the authors, the grade of acidosis can be measured in a subject by administering 2 grm. of sodium bicarbonate in 100 c.c. of water every half-hour, immediately preceding the dose by a test of the reaction of the urine. The 'first significant change in the urinary acidity' is taken as the end point, and the amount of alkali taken to produce this change measures the acidosis. In severe cases more than 2 grm. sodium bicarbonate is given at each dose. In normal and pathological cases, the plasma bicarbonate $CO_2$ during this process approaches $68{\cdot}7 \pm 10$ volumes of $CO_2$ at the time that the first depression of the urinary acidity is noted. There appears to be no close connexion between the function of regulating the acid-base equilibrium possessed by the kidney and its ability to excrete phenol sulphonephthalein. R. A. P.

**Sundstroem, E. S., and Bloor, W. R. Physiological effects of short exposures to low pressure.** *J. Biol. Chem.*, 1920, **45**, 153.

**Bloor, W. R. Blood phosphates in the lipaemia produced by acute experimental anaemia in rabbits.** *J. Biol. Chem.*, 1920, **45**, 171.

In the first paper, the authors have found that exposure of rabbits to low atmospheric pressures causes a decrease in size in addition to an increase in the number of erythrocytes. The phosphorus content of the red cells does not change, though there is a decrease in organic phosphorus in the plasma. There is a constant decrease in the lipoid phosphorus (lecithin) of the plasma, which is considered to be connected with an enrichment of the organs forming red blood corpuscles. Further, they think this decrease to have some connexion with the stimulation of these organs by the low atmospheric pressure.

In the second paper, the author has studied the distribution of lipoid phosphorus (the lecithin fraction) during the lipaemia produced by bleeding rabbits. His idea is to find out more about the function of the lecithins in metabolism, which are considered to bear an important part in the intermediary metabolism of fat. He finds that of all the phosphorus compounds in the blood, the lipoid phosphorus is most markedly affected by bleeding, being increased up to five times the normal in the plasma. This is accompanied by an increase in inorganic phosphorus, but no change in the other forms of phosphorus, so that the inorganic phosphorus and lipoid phosphorus seem to be directly related to one another. R. A. P.

**Haggard, H. W., and Henderson, Yandell. Haemato-respiratory functions. IX. An irreversible alteration of the $H_2CO_3/NaHCO_3$ equilibrium of the blood induced by temporary exposure to a low tension of $CO_2$.** *J. Biol. Chem.*, 1920, **45**, 209.

This is one of a series of four papers in the number of the Journal by the authors. In this paper, they show that the exposure of blood to a tension of $CO_2$ below a critical level causes the production of an irreversible change. After such an exposure the blood will not combine with as much $CO_2$ as normally, upon re-exposure to the normal $CO_2$ tension. Defibrinated blood shows this change more readily than oxalated blood. It is partly associated with bursting of the corpuscles, but there are other factors at work. (Possibly one of these is the development of lactic acid in standing blood recently described by Mellanby and Thomas.) R. A. P.

**Straub, H., u. Meier, Klothilde.** Blutgasanalysen. VIII. Der Einfluss einiger Digitaliskörper auf die Ionendurchgängigkeit menschlicher Erythrocyten. [**Blood gas studies. VIII. The influence of certain digitalis bodies on the permeability to ions of human red blood corpuscles.**] *Biochem. Ztschr.*, 1920, **111**, 67.

This is the eighth of a series of studies on the permeability changes of red corpuscles. The authors have found that the red corpuscles are impermeable to electrolytes in weakly basic solutions. As the acidity of the solution, in which the corpuscles are suspended, is raised, there becomes a sudden sharply defined point at which the corpuscles become permeable. The effect upon the inside of the cell is to allow the combination of acid ions with the haemoglobin enclosed in the cell. Other ions besides the hydrogen ion (acidity) influence permeability. The addition of potassium to the suspension fluid, for instance, makes the corpuscles permeable at a lower hydrogen-ion concentration (less acid reaction). This effect can be antagonized by calcium. The authors have interpreted their results in the sense that there is a change of condition of the cell surface by adsorption of the active ion. They, however, consider it misleading to picture a fine extracellular membrane as the affected layer. Their results can be interpreted rather as a change of state of the whole cell protoplasm.

As they were struck with the general correspondence between these permeability experiments and experiments upon the action of digitalis on the heart, the authors have tried the effect of adding digitalis to their blood-corpuscle suspensions. They found that digitalis had the effect of making the corpuscles become permeable at a more acid point than the normal in sodium chloride solution, thus resembling the effect of calcium ions. Potassium ions antagonized the effect. The result agrees with the pharmacological observation of the correspondence between the calcium and the digitalis effect. R. A. P.

**Linzenmeier, G.** Untersuchungen über die Senkungsgeschwindigkeit der roten Blutkörperchen. II. [**Investigations on the rate of sedimentation of the red blood corpuscles. II.**] *Arch. f. d. ges. Physiol.*, 1921, **186**, 272.

As in the blood in pregnancy, so also in the blood of various animals, sedimentation is retarded by shaking the plasma with kaolin, or by heating to 56° C., and is hastened by gelatin or gum. The sedimentation (which is due to the removal of the negative charge on the corpuscles) is also hastened by fibrinogen, histone, or protamine, but not by albumin, nuclein, sodium nucleinate, or peptone. The sedimenting factor in blood is probably not fibrinogen, but a definite fraction of the globulin. The bloods of different species show individual peculiarities in the sedimentation, which seems to be related not only to the alteration of the electric charge, but also to an adsorption of the agglutinating substances on the surface of the corpuscles. C. L. E.

**Abderhalden, E.** Die Beziehungen der Senkungsgeschwindigkeit der roten Blutkörperchen zu im Plasma vorhandenen diaylsierbaren Verbindungen; Beziehungen zu den Abwehrfermenten. [**The rate of deposition of erythrocytes in plasma and its relation to protective ferments.**] *Fermentforschung*, 1921, **4**, 230.

It has been known for some time that the corpuscles in the blood of pregnant women settle more rapidly than normal blood. Abderhalden has attempted to bring this phenomenon into relation with his much discussed pregnancy test. Linzenmeier's results showed that the change in rate of deposition occurred in those cases where the pregnancy test was positive. Abderhalden shows in the present paper that there are substances present in gravid blood which will cause normal corpuscles to sink more rapidly, and these substances may be removed by dialysis of the plasma. The plasma obtained from the umbilical cord does not behave like the maternal plasma. Certain peptones and amino-acids were examined for their influence on settling. No effect was made out. C. G. L. W.

**Coulter, C. B. The isoelectric point of red blood cells and its relation to agglutination.** *J. Gen. Physiol.*, 1921, **3**, 309.

The H-ion concentration at which red corpuscles have no electric charge is at $P_H = 4 \cdot 6$. On the alkaline side of this, they are negative; on the acid side, positive. The charge carried by sensitized cells on the alkaline side is smaller than that of normal cells. On the acid side, both kinds of cells 'combine' with H and Cl ions; on the alkaline side with cations. The optimum for agglutination of normal cells is at $P_H = 4 \cdot 75$; for sensitized cells, at $P_H = 5 \cdot 3$. The latter value is related to the optimum for flocculation of the immune body. W. M. B.

**Vorschütz, J.** Untersuchung über Agglutination und Sedimentierung von Bakterien. **[Investigation on the agglutination and sedimentation of bacteria.]** *Arch. f. d. ges. Physiol.*, 1921, **186**, 290.

Certain bacteria, but not all, are agglutinated by the serum of pregnant women under the same conditions as are red blood corpuscles. It is inferred that the fundamental physico-chemical phenomena are also similar, viz. that sedimentation is preceded by the removal of the electric charge on the organisms in suspension. C. L. E.

**Hess, A. F.,** and **Unger, L. J. Dietaries of infants in relation to the development of rickets.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 220.

In an examination of infants on various diets, which were continued for six months, it was found that many diets supposed to be conducive to rickets resulted in normal nutrition. Condensed milk only occasionally produced rickets. The one food which regularly caused the condition was 'protein milk' prepared by precipitating buttermilk with heat (not with rennin). This preparation contained 3·3 per cent. of protein, 25 per cent. of fat, and 6·6 per cent. of carbohydrate. Its ash was about 0·44 per cent., of which the phosphorus and calcium content stood midway between human and cows' milk. The fat-soluble vitamine content was high, the water-soluble vitamine low. This diet must be regarded as one markedly productive of rickets. All the infants received an adequate supply of orange juice during the period of feeding. C. G. L. W.

**McCollum, E. V., Simmonds, N., Parsons, H. T., Shipley, P. G.,** and **Park, E. A. Studies on experimental rickets. I. The production of rachitis and similar diseases in the rat by deficient diets. II. The effect of cod-liver oil administered to rats with experimental rickets.** *J. Biol. Chem.*, 1921, **45**, 333 and 343.

These interesting papers form, so the authors say, the beginning of a series. By uniting the interest of the Chemical Hygiene Department and the Department of Pediatrics of Johns Hopkins University, it has been possible to initiate an intensive study of the dietary and pathological sides of rickets in rats.

Diets faulty either in calcium or fat-soluble A especially, or deficient in certain other ways, have been found to induce disturbances in the growth of the skeleton such as fractures, enlargement and distortions of the costo-chondral junctions, vertebral deformity, irregularities in the calcification of the intercellular substance of the proliferative cartilage. The authors lay stress upon the difficulty at this stage of drawing conclusions, though it is interesting that calcium and fat-soluble vitamine seem to be the most prominent factors. In the second paper of the series, a preliminary one, they claim that the feeding of cod-liver oil to rats suffering from lack of fat-soluble vitamine induces the deposition of calcium salts between the cells of the proliferative zone of cartilage. This line suggests a means by which cod-liver oil produces its effects in the treatment of rickets. (It is surprising that the work of E. Mellanby should not be mentioned by the authors). R. A. P.

**Dutiker, R. A., Eckles, C. H., Dahle, C. H., Mead, S. W.,** and **Schaefer, O. G. Vitamine studies. VI. The influence of diet of the cow upon the nutritive and antiscorbutic properties of cow's milk.** *J. Biol. Chem.*, 1920, **45**, 119.

The vitamine content of cow's milk is dependent upon the vitamine content of the ration ingested by the cow. 20 c.c. of summer milk were superior to 60 c.c. of winter milk in antiscorbutic potency and nutritive value. Milk becomes poor in vitamine slowly, but the vitamine is quickly restored when the animal is fed on a vitamine rich diet. R. A. P.

**Osborne, T. B.,** and **Mendel, L. B. A critique of experiments with diets free from fat-soluble vitamine.** *J. Biol. Chem.*, 1921, **45**, 277.

The authors draw attention to the contradictions existing in the literature as to the presence or absence of fat-soluble vitamine in a given experimental diet. They instance some results of Daniels and Loughlin in which the conclusion was drawn that rats could be made to grow, reproduce and rear their young upon a diet 'in which the only apparent source of vitamine was lard or cotton-seed oil'. Other workers have concluded that lard is not a source of fat-soluble vitamine. In many experiments it has been found that in the apparent absence of a supply of fat-soluble vitamine, animals will grow quite well for a time before failure. Results of this kind have been attributed either to 'exceptional vitality' or to a possession of a reserve store of vitamine in the body. By extracting carefully the other constituents of the diet, viz., proteins and carbohydrates, the authors have been able to diminish to some extent the period of unrestricted growth upon diets deficient in fat-soluble vitamine. They are inclined to think that the discordant results of various workers may perhaps be due to traces of fat-soluble vitamine adhering to proteins, &c., in the diet. However, they point to the fact that the crucial experiment in which nutritive failure ensues immediately upon giving a diet deficient in this respect has not yet been done. R. A. P.

**Osborne, T. B.,** and **Mendel, L. B. Growth on diets poor in true fats.** *J. Biol. Chem.*, 1920, **45**, 145.

Rats fed on a diet in which the largest fat intake daily per animal was not more than 0·078 grm. grew well. This indicates that if 'true fats are essential for nutrition during growth, the minimum required must be exceedingly small'. In all cases, a source of fat soluble vitamine was added. R. A. P.

**Drummond, J. C. Nutrition on diets practically devoid of fat.** *J. Physiol.*, 1920, **54**, xxx.

The accessory food factor A (fat-soluble A), was supplied by an alcoholic extract of fresh carrots containing only the smallest traces of neutral fat. The basal ration was composed of caseinogen and starch (both extracted with alcohol and ether), inorganic salts, orange juice and yeast extract. To this a daily ration of 5 c.c. of the concentrated carrot extract was added. The approximate daily intake of neutral fat was 14 milligrammes. Young rats remained in good health on this diet for nearly six months, and showed considerable, though, on the whole subnormal, growth. O. L. V. de W.

**Witzemann, E. J. Disodiumphosphate as a catalyst for the quantitative oxidation of glucose to carbon dioxide with hydrogen peroxide.** *J. Biol. Chem.*, 1920, **45**, 1.

This paper is of considerable interest in connexion with carbohydrate metabolism. The author has confirmed and extended some results of Löb. The latter showed that in the presence of phosphates glucose was oxidized by hydrogen peroxide to $CO_2$ and $H_2O$. The author has found that, at the temperature reaction of the body, glucose is oxidized in the presence of disodium phosphate by hydrogen peroxide, the phosphate apparently acting as a catalyst. Compounds of hexoses and phosphate (hexose-phosphate) have been described by Harden and Young, Neuberg, and others, in connexion with the fermentation of yeast, and also with the precursors of lactic acid in the muscle. Thinking that a hexose-phosphate might be playing an intermediate part, the author tried to isolate such a compound, without success. R. A. P.

**Cushing, H.,** and **Foley, F. E. B. Alteration of intracranial tension by salt solution in the alimentary canal.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 217.

Weed and McKibbon (*Am. J. Physiol.*, 1919, **48**, 531) have shown that it is possible to reduce the cerebrospinal fluid pressure, and diminish the bulk of the brain by injecting a hypertonic salt solution into the bloodstream. Hypotonic solution had the opposite effect. Cushing and Foley have confirmed these results and have attempted to achieve them in another way. By introducing 20–30 c.c. of a saturated solution of sodium chloride into the rectum or duodenum of a cat, a maximal fall of cerebrospinal pressure was produced as if the solution were given intravenously. The experiments were repeated with patients with brain tumours and cerebral herniae subsequent to decompression operations. Occasionally very striking results were obtained in which a tense convex protrusion became a soft concave area over the decompression site. C. G. L. W.

**Cheplin, H. A.,** and **Rettger, L. F. Further studies on intestinal implantation of *Bacillus acidophilus*.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **18**, 30.

The preparation of *B. acidophilus* milk is conducted by using mixed strains of the bacillus which have been grown sufficiently long on milk to bring about light curdling within 24 hours. If the milk is more or less acid before sterilizing, the final product is of an even consistency, granular and lumpy.

Successfully prepared acidophilus milk is of uniform creamy consistency. The odour is slightly aromatic. The acidity is always below 1·0 per cent. Samples of milk which have been kept at room temperature for two weeks are practically indistinguishable from the fresh product. The clinical results in effecting a transformation of the flora of the intestine by the use of the milk have been most promising. C. G. L. W.

**Uhlenhuth, E. Experimental gigantism produced by feeding pituitary gland.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **18**, 11.

By feeding the anterior lobe to salamanders specimens were produced which attained a growth much larger than any which have hitherto been seen. If the animals are fed on the posterior lobe, growth may be greatly retarded. Feeding produces both acceleration of growth and continuation beyond the specific size of the species. C. G. L. W.

**Cameron, A. T.,** and **Carmichael, J. Biochemistry of iodine. III. The comparative effects of thyroid and iodide feeding on growth in white rats and in rabbits.** *J. Biol. Chem.*, 1920, **45**, 69.

The effect of feeding continued small doses of desiccated thyroid gland to young white rats was threefold. There was a definite decrease in the growth-rate, a hypertrophy of the heart, liver, kidneys, and adrenals, and a disappearance of fat. The latter two results confirm those of Hoskins and Herring. The decrease in rate of growth is proportional to the amount, and also to the iodine content, of the thyroid tissue fed. The hypertrophy, varying with the dose and length of duration of the feeding, is proportional to the iodine content. The feeding of sodium iodide does not reproduce these effects, nor does the extract of other glandular tissues. R. A. P.

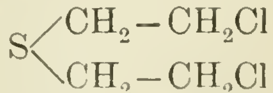
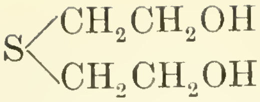
**Uhlenhuth, E. Experimental production of gigantism by feeding the anterior lobe of the hypophysis.** *J. Gen. Physiol.*, 1921, **3**, 347.

Metamorphosed salamanders (*Ambystoma opacum* and *tigrinum*) grew much more rapidly on anterior lobe of hypophysis than did controls on earthworms. Experimental giants were produced. W. M. B.

**Pézard, A. Numerical law of regression of certain sex characters.** *J. Gen. Physiol.*, 1921, **3**, 271.

Post-puberal castration in cocks results in a regression of the comb similar to that effected by castration before puberty. The rate of diminution is represented by a segment of a parabola. W. M. B.

**Rona, P.,** u. **Petow, H.** Giftwirkung des Thiodiglykols und seiner Derivate an Sojabohnenurease. [**Poisonous effect of thiodiglycol upon urease.**] *Biochem. Ztschr.*, 1920, **111**, 134.

These experiments have some interest in connexion with the toxic effect of mustard gas. Mustard gas, or dichlor-diethyl sulphide  $S\left\langle\begin{matrix}CH_2-CH_2Cl\\CH_2-CH_2Cl\end{matrix}\right.$ is (as has been demonstrated recently), very toxic in its effects, whereas thiodiglycol,  $S(CH_2CH_2OH)_2$ is practically not poisonous. The curious fact is that the former substance in water rapidly passes into the latter with splitting off of Cl. It has always been difficult to relate the toxic effect of the chlorine derivative in the body to its chemistry. The authors here have found an analogy in the effect of the two substances upon the ferment urease. This ferment splits urea to ammonia and $CO_2$. Thiodiglycol does not poison the ferment, whereas dichlorethyl sulphide stops the action of urease even when used in quite small quantities. R. A. P.

**Biberfeld, J.** Zur Kenntnis der Gewöhnung. IV. Über Gewöhnung an Kodeinderivative (Eukodal u. Parakodin). [**On acclimatization to drugs. The acclimatization to codein derivatives (eucodal and paracodein).**] *Biochem. Ztschr.*, 1920, **111**, 91.

The author concludes that eucodal depresses the respiration more than morphin, though the former is less poisonous than heroin.

Rabbits do not get accustomed to doses of eucodal. In dogs the sedative effect soon wears off by repeated injection, and is replaced by an excitant effect for larger doses. Paracodein has a stronger effect upon respiration than codein, weaker than eucodal and morphin; dogs show an acclimatization to the sedative component of the effect. R. A. P.

**van der Willigen, A. M. M.** Die Abführwirkung des Schwefels. Die Abführwirkung des Kalomels. Die Abführwirkung des Phenolphthaleins. [**The purgative action of sulphur—of calomel—of phenolphthalein.**] *Arch. f. d. ges. Physiol.*, 1921, **186**, 173, 185, 193.

Experiments were made on cats, by the bismuth meal and X-ray method, before and after the administration of the various cathartics. Some experiments were also made on isolated loops of intestine. The action of sulphur was shown to be due to the effect of sulphuretted hydrogen produced from it in the large intestine (and passed in the flatus). The movements of the proximal colon are so accelerated by the sulphuretted hydrogen that the normal absorption of water in that portion of the bowel is much reduced. No sulphuretted hydrogen was detected in either the expired air or blood after administration of sulphur. The absorptive and secretory activities of the intestinal mucosa were unaltered. Calomel hastens the passage along both small and large intestines, and likewise leaves secretion and absorption unaffected.

Phenolphthalein chiefly stimulates the colon, and to a much smaller extent the small intestine, and does not affect either secretion or absorption. C. L. E.

**Schulz, W.** Der Verlauf der Kreatininausscheidung im Harn des Menschen mit besonderer Berücksichtigung des Einflusses der Muskelarbeit. [**The course of creatinin excretion in the urine in man, with especial reference to the effect of exercise.**] *Arch. f. d. ges. Physiol.*, 1921, **186**, 126.

The daily creatinin excretion is moderately constant on a creatin-free diet, and is independent of the volume of urine passed. It falls steadily during starvation. During the day there are three maxima, at about

10 a.m., 2–4 p.m., and 8–10 p.m., and these are unaltered in starvation. Creatin is absent except during starvation. During muscular exercise, whether in the fed or fasting subject, there is a rise in the creatinin output, but the daily excretion is unaffected. C. L. E.

## RADIOLOGY

### *Radio-technique*

**Taylor Jones, E. The action of induction coils.** *J. Rönt. Soc.*, 1920, **16**, 47.

The paper deals mainly with variations in the wave-form of potential at 'break', consequent on the variation of the frequency-ratio of an induction coil. The first part of the paper is based on the theory that when the secondary terminals are insulated the wave-form of potential after 'break' consists of two components which begin in opposite phase and the initial amplitudes of which are inversely proportional to their frequency. The author shows that the maximum potential cannot exceed the sum of the amplitudes and can only attain this value for frequency-ratios 3, 7, 11, &c.

The frequency-ratio of a coil is smallest when the primary capacity is such that $L_1C_1 = L_2C_2$, its value then depending on the coupling. For still smaller values of the primary capacity the frequency-ratio steadily increases, and it is to this range that the author restricts himself.

By withdrawing the primary and core to various distances along the axis of the secondary and consequently altering the coupling, it was found that the spark length produced at the interruption of a given primary current was a maximum when the primary was about 1 foot from its normal position. The coupling was found to be 0·58 for this position of the primary coil. The experimental curve, showing the way in which the secondary potential varies with the primary capacity, is well in accord with theory except that the potential is reduced considerably by the damping. In actual coils the least efficient coupling appears to be rather smaller than the corresponding value for a coil devoid of damping. The author's experiments show that the spark length for an 18-inch coil does not necessarily increase with the mutual inductance, and that the effect of damping in reducing the secondary potential increases with the coupling, amounting in some cases to a 25 per cent. reduction.

A description is given of an electrostatic oscillograph capable of being used up to 200,000 volts, and some examples of the photographs obtained with it illustrate remarkable agreement between theory and experiment. Other wave-forms, obtained when the oscillograph was connected to the terminals of a fairly soft X-ray tube, suggest that the latter is behaving like a resistance which, while greater than that of a spark of moderate length, is still sufficiently small to be non-oscillatory. A hard tube follows more closely the nominal form when the terminals of the coil are insulated.
L. H. C.

**Phillips, C. E. S. A suggested new method of measuring X-ray dosage.** *Arch. Radiol. & Electroth.*, 1920, **25**, 215.

The main feature of the suggested ionization method is the use of a thermionic valve which enables small variations of current in an ionization chamber to be transformed 'up' to give corresponding variations of a much larger current in a separate circuit at low tension. The recording instrument is a milliampere-meter which is included in the separate circuit.

The ionization chamber is hermetically sealed and has two, parallel plate, electrodes, the lower resting in a bed of ebonite and connected by a short, heavily insulated wire to the grid of the valve.

The author describes the action of the thermionic valve and states that the recording instrument should give steady readings, which will vary with the intensity of radiation. L. H. C.

## *Radio-diagnosis*

**Dandy, W. E. Localization or elimination of cerebral tumours by ventriculography.** *Surg. Gynec. & Obst.*, 1920, **30**, 329. (*J. de radiol. et d'électrol.*, 1920, **11**, 520.)

It is very difficult to localize cerebral tumours clinically unless they are large, but it is only by exact localization that they can be removed. Radiography of the ventricles consists in passing into one of the lateral ventricles a needle through which air is injected after the removal of some of the cerebrospinal fluid, after a preliminary small trephining under a local anaesthetic. A series of X-ray photographs is then taken from different positions in such a manner that the various parts of the ventricle in turn may contain the air. Every cerebral tumour alters the shape of the ventricle. By this method an early diagnosis, and therefore an early removal, of the tumour can be made. P. L.-B.

**Duval, P., Roux, et Beclère, H.** L'ulcère de la petite courbure de l'estomac. [**Ulcer of the smaller curvature of the stomach.**] *Arch. d'électric. méd.*, 1920, **28**, 289.

An ulcer of the lesser curvature presenting Mathieu's syndrome can be definitely diagnosed by X-rays.

(1) Under the X-rays there are two modifications of the lesser curvature: (*a*) a portion of the lesser curvature becomes straight; (*b*) a diverticulum of Haudek. The straight portion varies in extent, but is always at the periphery of the ulcer and corresponds to the point which is painful on palpation. A typical diverticulum of Haudek indicates an ulcer which has invaded the perigastric tissues.

(2) Modifications of the larger curvature consist of an indentation in the wall and sometimes in a mixed biloculation. The indentation always occurs in the same place; its usual position is opposite the ulcer. It may be the only sign of an ulcer. Differential diagnosis between this and functional or cicatricial contractions is given.

(3) The general appearance of the stomach is modified in several ways. The action of the pylorus should be closely examined. The author classifies the X-ray appearances of the ulcers thus: (*a*) commencing ulcer;

(*b*) definite ulcer without perforation or contraction; (*c*) punched out ulcer with projecting edges; (*d*) ulcer with mixed biloculation. The signs of these various types are given. It is stated that radiology alone is insufficient, but combined with clinical observation is of the greatest value. An X-ray photograph is not enough; examination under the screen must be undertaken and the radiologist and physician or surgeon must collaborate.

P. L.-B.

**Spriggs, E. I. Duodenal diverticula.** *Brit. J. Surg.*, 1920, **8**, 18.

In a thousand consecutive X-ray examinations of the alimentary tract, duodenal diverticula have been seen ten times; they rarely gave rise to symptoms. The shadows may cause confusion unless their nature is realized and the contents are seen passing into the duodenum. The size varies from a linseed to a hen's egg. The commonest situation is the second part of the duodenum, of which the region of the ampulla of Vater is the favourite site.

P. L.-B.

**Cole, L. G., and Roberts, D. Duodenal diverticula; their clinical and radiological aspect.** *Surg. Gynec. & Obst.*, 1920, **31**, 376. (*Arch. d'électric. méd.*, 1920, **28**, 364.

Up to a few years ago diverticula of the intestine were scarcely recognized. Those of the large intestine were the first and best studied, the rest being looked upon as curiosities. Cole and Roberts show that duodenal diverticula occur more frequently than was thought. They occur particularly in the region of the ampulla of Vater and develop there at the expense of the posterior wall or of the lumen of the duodenum. Diverticula of the first part are very rare, but less so than those of the third or fourth parts. Single, or in groups of three or four, the size varies from that of a nut to that of a pear: the opening is large or narrow, and the interior sometimes contains food débris.

Their presence entails certain symptoms and complications, such as intestinal obstruction, persistent indigestion, regurgitations of food, which may be haemorrhagic and chronic; the authors also think that diverticula are not unconnected with primary cancer of the duodenum, rare though it be.

On radiological examination, the fact that the meal remains in these pouches, reveals their presence: most often, however, the opaque meal only confirms their presence and their anatomical grouping, whether round the ampulla of Vater or not. The diagnosis, however, always remains very delicate, because in the presence of shadows visible before an opaque meal it will be necessary to bear in mind renal, biliary, and pancreatic calculi, calcified mesenteric or retro-peritoneal glands, or faecal concretions. When the opaque meal has been taken, it will be necessary to think of dilatation of the first part of the duodenum accompanying a duodenal ulcer; perforating ulcers; fistulae between duodenum and gall-bladder; further, it must not be forgotten that, in a patient who has taken a bismuth or barium meal, intestinal shadows due to particles of these substances can be seen for several days.

Also, owing to the difficulty of such a diagnosis, one examination is not

sufficient. Many should be made, and only after a very careful comparison of the results has been made can the existence of a diverticulum be affirmed.
P. L.-B.

**Ramond, F.** Le spasme du pylore. [**Pyloric spasm.**] *Presse méd.*, 1920, May. (*Arch. d'électric. méd.*, 1920, **28**, 344.)

In its complete form spasm of the pylorus shows itself by the following radiological signs: at the moment of its arrival in the stomach, a part of the opaque meal passes into the duodenum by 'surprising' the pylorus. Contraction having taken place, the closed pylorus appears as a light band, clearly seen above the horizontal plane, passing through the fundus of the stomach. Above may be seen an immobile column of bismuth with no tendency to empty itself either into the duodenum or into the stomach. After a time, sudden relaxation of the sphincter supervenes, and the bismuth mass is either forced precipitately into the duodenum, or passes little by little. At the same time the duodenal column separates into two portions, one part progresses towards the second part of the duodenum, while a small amount of bismuth returns into the stomach. In a less vigorous form of pyloric spasm, the pyloric region is always clearly visible, but it allows a fine opaque thread to pass; the duodenal column is not so high, and the duration of the phenomenon is shorter.

It is possible to bring the spasm still better into relief: (1) by manual compression of the pyloric region, with the object of forcing open the sphincter, the resistance of the pylorus is more prolonged and sometimes absolute; (2) a spoonful of syrup of belladonna or an injection of 1 mg. of atropin brings about cessation of the spasms (this test sometimes fails); (3) a cachet of 50 cgrm. of adrenal ingested a quarter of an hour before examination often reveals a latent spasm, or exaggerates it if it be already in existence; the patient experiences painful cramp and the screen shows a good image of the spasm. S. U. L.-B.

**Hinman, F.** Diverticules vésicaux. [**Diverticula of the bladder.**] *Surg. Gynec. & Obst.*, 1919, August. (*Arch. d'électric. méd.*, 1920, **28**, 345.)

Cystoscopy and radiography have shown that vesical diverticula are much more frequent than was believed, and from 21 personal observations the author draws the following conclusions:

The largest proportion is furnished by men between the ages of 50 to 60 years; women are nearly always exempt, the author only having observed two cases.

Three different examinations are necessary to make an exact diagnosis of this affection. The first by cystoscopy, the second by radioscopy, the bladder having been previously filled with an opaque liquid, and the third by radiography. As this last examination must serve to differentiate between the vesical cavity and the diverticula and to indicate the seat of the orifices which connect them with the bladder, it can only be made after having emptied the vesical cavity and replaced its opaque contents with an injection of air. In this way will be shown, in positive cases, a light mass formed by the bladder, crossed by the shadow of the diverticula which still contain the opaque liquid.

According to the author, a single diverticulum is most often found and in this case it borders on the ureteral orifice. In the case of multiple diverticula they are seen at the base of the bladder and their volume is then less than in the case of a single diverticulum. From the clinical point of view the symptoms are vague and dominated by the phenomena of prostatic lesions which almost always accompany diverticula. Diagnosis can only be made by cystoscopic and radioscopic examination. S. U. L.-B.

## *Radio-biology*

**Russ, S. Some problems in the biological action of radiations.** *J. Rönt. Soc.*, 1920, **16**, 134.

In treating, say a rapidly growing tumour, one of the greatest difficulties in administering a lethal dose is that the cells are in different stages of activity. It might be thought that a rapidly growing tumour would be more vulnerable than one growing slowly, but this is not always the case: the response also depends on the type of cell. If a tumour disappears after radiation it may do so because of chemical or physical processes, but which is the more important is not known.

In carrying out experiments *in vivo* and *in vitro,* the results may be widely different or the same: experiments on lymphocytes after radiation vary greatly *in vivo* and *in vitro,* whereas those on Jensen's rat sarcoma give almost identical results. The former may be an action on the exterior of the cell and on its surrounding, while the latter is almost certainly on the internal structure of the cell.

There may be two variables, (*a*) the cell, and (*b*) the radiation. As yet the energy of radiation from one part of the spectrum with that of another cannot be compared.

The biological reaction of a tissue bears no simple relation to the amount of energy absorbed when exposed to different parts of the spectrum. It may be significant that the U.V., X-rays, and $\gamma$-rays, which give the most pronounced biological actions, are those which give rise to the most marked electronic emission.

The electronic emission probably gives rise to physical rather than chemical conditions, as chemical changes are only seen after heavy doses, while numerous physical effects can be seen after small doses. Electrical forces play a considerable part in many processes. It has been shown for several types of cell that the same amount of energy from $\beta$- and $\gamma$-rays will produce similar results. P. L.-B.

**Bagg, H. J. The response of the animal organism to repeated injections of an active deposit of radium emanation. Intravenous injections in dogs.** *Am. J. Cancer Research*, 1920, **5**, 301.

The animals were two bitches, one a Dalmatian, the other a mongrel. Complete urine analyses were made before and after treatment; frequent blood examinations were made, temperature and weight recorded, and histological examinations made of post-mortem specimens.

The active deposit consisted of a solution in which radium emanation had been deposited on NaCl, which was later dissolved in sterile water to make a physiological salt solution.

The injections were made into the veins of the ear, about 2 c.c. being injected at a time. The syringe was lead covered. A second injection was not made until the metabolism had recovered.

Blood examinations were made from the ear. Temperatures taken in the rectum.

*Dog I.* Experiments lasted for three months; four injections were made totalling 231·8 mc. The first injection was of 95·3 mc., after which the animal was affected for two days; the second injection a month later was apparently without effect except for loss of appetite on the 13th, 23rd, and 24th days.

After the first injection the leucocytes fell in number till the eleventh day, from 10,250 to 4,200; from then onwards there was a steady recovery. After the second injection the white cells again fell, but the red slightly increased in numbers. On the eleventh day there was a marked decrease in the polynuclears with a rise in the lymphocytes, but the differential count was normal before the second injection. After the injection there an increase in the total nitrogen and urea and a considerable increase in the uric acid and phosphates in the urine.

The second injection was made on the thirty-first day; the dose was 30 mc. The faeces became slightly fluid, otherwise the animal was normal. The temperature was low and irregular for a few days. After 3 days the leucocytes were slightly raised, but later fell to about 75 per cent. The red cells fell slightly at first.

The third injection was made on the forty-second day; the dose was 42 mc. There followed diarrhoea and loss of appetite for 10 days and the animal lost 2 lb. in weight. The temperature rose sharply and was high and irregular for several days. On the third day after injection the leucocytes had fallen to 2,900 but increased to 12,500 before the next injection: Hb. 80 per cent. The red cells increased in number to nearly a million more than normal before the fourth injection. The blood clotted rapidly. The urine contained an increase of total nitrogen, urea, uric acid, creatinin, and total phosphates.

The fourth injection was made on the sixty-fifth day; the dose was 64·5 mc. It was followed by severe vomiting, constipation, and a sudden rise of temperature to 102°. The animal refused food for two days and was seriously ill; there was a loss of weight of 3¼ lb. The white cells fell to 5,600, the red cells fell slightly. There was a relative increase of lymphocytes and fall of polynuclears. The excretion of urine was increased.

Histologically there was an intensely congested liver with granular degeneration. The kidneys were congested and showed degeneration of the tubule cells. The Malpighian bodies of the spleen were prominent, few cells in the pulp. The colon was congested. The lymph nodes were congested. The lymph follicles decreased in size. No changes were noted in lungs, stomach, small intestine, or thyroid.

*Dog II.* Experiments lasted two months. Four injections were given totalling 338·4 mc. The first injection was followed by a low and irregular temperature for several days. Vomiting occurred after three days. The animal refused food and lost 2 lb. in weight in six days. The leucocytes fell from 14,400 to 2,150 in seven days. The red cells fell by nearly two million, causing a fall of Hb. from 85 to 75 per cent. There was a large increase of uric acid and total phosphates in the urine.

The second injection was made on the twenty-eighth day; the dose was

17·3 mc. After an initial fall, the temperature rose to 102·5° on the second day. There was a decrease in the white cells, but the red cells increased slightly in numbers. There was only a slight increase in the total nitrogen, uric acid, &c.

The third injection was made on the thirty-seventh day; the dose was 54·7 mc. The temperature rose slightly for three days; on the fourth day the animal refused food and lost $1\frac{1}{2}$ lb. in weight. There was a relative decrease of the lymphocytes and increase of the polynuclears. There was an increase of total nitrogen and phosphates in the urine; the creatinin remained constant.

The fourth injection was made on the fifty-second day; the dose was 146·4 mc. The temperature was high before injection but soon fell. A few hours after the injection there was vomiting and the passage of semi-solid faeces. Food was refused. The animal lost 2 lb. in weight in five days and was seriously ill. The white cells fell to 1,400 with a great reduction in the lymphocytes to 3 per cent.; the polynuclears increased to 95 per cent.

Histologically there were fatty and granular degeneration of the liver, congestion of the kidneys, and slight degeneration of the tubule cells. The splenic cells were pigmented and the follicles small and scanty, the organ was congested and fibrosed. In the bone marrow of the head of the femur, fat replaced the lymphoid cells. The pancreas, thyroid and parathyroids, stomach, and small intestine showed no change.

The experiments show that the same effects on the blood may be obtained by the intravenous injection of the active deposit of radium emanation as by X-rays, and that definite physiological reactions follow the injections.

*Conclusions.* Large intravenous doses produced a large drop in the leucocytes up to 80 per cent., and a reduction of the red cells to about 25 per cent. Repeated injections apparently produced a marked decrease of lymphocytes. Injections produced severe digestive disturbances and a marked drop in body-weight. In many cases there was a rise in temperature, probably in response to a toxic condition. The larger doses were followed by great increase in the total nitrogen, urea, &c., in the urine. Relatively small doses, after the organism had been injured, produced definite changes.

Histologically there was great congestion of the principal viscera.

When treating patients the dose must vary according to the physical condition and a second dose should be smaller than the first.

P. L.-B.

**Cluzet, Rochaix, et Kofman.** Action bactéricide du radium sur le bacille pyocyanique. [**The bactericidal action of radium on *B. pyocyaneus*.**] *Réunion biologique de Lyon.*, 1920, July. (*J. de radiol. et d'électrol.*, 1920, **4**, 525.)

This is a very important piece of work from the point of view of radio-biology. The authors, using a tube with walls of 0·5 mm. of platinum, have employed a higher proportion of gamma-rays than that ordinarily used in physiological experiments. These tubes, indeed, allow less than half the beta-rays and almost all the gamma-rays to pass through.

The tube used by them contained 50 mg. of $RaBr_2 . 2H_2O$, that is, about 25 mg. of radium element.

They did not determine the intensity of the field around the tube and in the various layers of the cultures, and as the culture tubes measured 1 cm. in internal diameter, they were forced to have fields of action differing greatly according to distance, therefore the following results can only be regarded as mean figures. This does not lessen their value.

The first experiment was on a 24-hours' culture of *B. pyocyaneus* in peptone broth. The irradiation lasted three days at a temperature of 16°C. The action of radium under these conditions was nil.

A second experiment made at room temperature with tubes immediately after inoculation, and seven days' irradiation, clearly showed a delay of twelve days in growth of the culture.

The third experiment was made on cultures kept in ice. These cultures were also kept in a living but arrested condition. Nine days' irradiation under these conditions sterilized the culture. That is, a drop of the irradiated culture when re-inoculated remained sterile, whereas a drop of a control culture kept at the same temperature during the nine days began to grow.

A control experiment has elsewhere shown that the retarding or sterilizing action is direct and is not produced indirectly through a chemical reaction on the medium.

From these experiments the authors conclude: (1) that radium appears to be without action when acting for 24 hours after inoculation; (2) that the action of radium on young cultures just beginning to grow is only retarding; (3) that if the growth of the culture is retarded by cold, the action of radium is clearly bactericidal. These results are comparable with those obtaining in seeds under the action of radium. P. L.-B.

# MEDICAL SCIENCE

## ABSTRACTS & REVIEWS

VOLUME IV. NUMBER 3 JUNE 1921

## CONTENTS

REVIEWS:

PAGE

TYPHUS . . . . . . . . . . . . . . . . 191

WHOOPING-COUGH . . . . . . . . . . . . . . 201

VACCINATION . . . . . . . . . . . . . . . 205

GONORRHOEA . . . . . . . . . . . . . . . 210

CHANCROID . . . . . . . . . . . . . . . 218

SURGICAL TREATMENT OF CHRONIC INTESTINAL STASIS . . 221

MELANIN, MELANOMA, MELANOTIC CANCER . . . . . . 229

ACUTE SUPPURATION ABOUT THE WRIST TREATED BY INCISION DIVIDING THE ANNULAR LIGAMENT . . . . . . . . 236

ABSTRACTS:

SURGERY . . . . . . . . . . . . . . . 239

NEUROLOGY . . . . . . . . . . . . . . . 242

PATHOLOGY AND BACTERIOLOGY . . . . . . . . . . 255

BIOCHEMISTRY . . . . . . . . . . . . . . 273

RADIOLOGY . . . . . . . . . . . . . . . 283

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# REVIEWS

## TYPHUS

**Epidemiology.** According to Hunter, the Serbian epidemic of 1915 was the most sudden in origin, greatest in extent, and most quickly arrested of any epidemic of a like kind in history. It lasted for about six months and maintained its maximum for about two months. Other epidemics have lasted 1½–3 years, and maintained their maximum for periods of 12 (Irish) or 18 months (English epidemic). Like the Irish epidemic of 1846–1848, the Serbian epidemic was one of relapsing fever and typhus combined. The first in origin was relapsing fever, the number of cases in hospital at the end of December 1914 being 2,184 as compared with only 200 of typhus. By the end of January the numbers of relapsing fever and typhus cases were 5,122 and 1,100 respectively, by the end of February 7,000 and 4,000 respectively, and by the end of march 8,100 and 8,000 respectively. Thereafter the proportions altered; at the end of April there were 3,260 cases of relapsing fever and 6,300 of typhus, and by the end of May 1,600 of relapsing fever and 2,860 of typhus. The mortality was 30 per cent. in January and February, and rose in a week or two to 40 per cent. in March. As usual, it was highest among the doctors; out of an original total of 450 Serbian doctors 100 died and 200 were rendered unfit for duty.

Cantacuzène draws attention to two remarkable features of the Roumanian epidemic of 1917–18. In the first place, concurrently with the outbreak of typhus, an abnormally virulent epidemic of relapsing fever developed, and both epidemics reached their highest incidence and mortality at the same time. The epidemic of relapsing fever rapidly declined in April 1917, and ceased entirely at the beginning of May, whereas the epidemic of typhus did not come to an end till June. The second remarkable feature of the epidemic was the fact that scarlet fever, which is usually extremely frequent and severe in Roumania, almost entirely disappeared during the epidemic of typhus. The average mortality in the Roumanian epidemic in the hospitals at the front and at the base was 15–17 per cent., ranging from 12–27 per cent. according to the various hospital centres. In the medical staff the mortality was 41 per cent., death being due in the great majority of cases to the bulbo-pontine form of the disease (*vide* also *Medical Science* 1920, **1**, 561).

According to Goodall, for the period January 1, 1916, to December 31, 1919, there were at least 431,200 cases of typhus in Congress Poland and Galicia combined. The number was probably higher, for there was little doubt that not a few cases escaped being recorded. During January and February 1920, 12,098 cases were notified in Congress Poland and 34,476 in Galicia. The epidemic was widely spread and prevailed at one time or another, with varying attack rate, all over Poland in 1918. Early in 1919 the whole country was more or less invaded, but the districts which suffered most were those in the east and south-west. Galicia and Volhynia were also severely affected.

Ruysch states that prior to 1918 typhus made only a sporadic appearance in Holland, only 9 cases having occurred between 1911 and 1917. This was all the more remarkable as in several neighbouring countries the disease was more or less prevalent, and thousands of persons had been crossing the frontier from infected areas ever since the first year of the war. In 1918 the first cases of typhus in Holland, which occurred at Amsterdam, were not recognized as such and were diagnosed as typhoid fever. A few days after admission to hospital the true nature of the disease was discovered both by clinical examination and the Weil-Felix reaction. It is probable that the late diagnosis favoured the extension of the epidemic. 17 cases occurred at Amsterdam and 40 at Urk, a little island in the Zuider Zee (vide *Medical Supplement*, 1919, **2**, 264). The character of the epidemic in 1918 was mild, but in January 1919 it assumed a more severe form, 20 districts being attacked. 120 cases occurred in January, 400 in February (a large number of these being in Rotterdam, Haarlem, and Delft), 300 in March, and 13 in April. The last case occurred on May 1. From January 1–May 1, 1919, there were 541 cases at Rotterdam, of which 87 were fatal. The mortality increased with the age of the patient, being nearly 50 per cent. between 60 and 74.

The epidemic of typhus in Rotterdam during the early part of 1919 is described by Kramer (1). The disease broke out with great suddenness and rapidly spread all over the town. In the week January 26–February 1, 6 cases were notified, and in the following weeks 126, 145, 170, and 119. As the result of the measures taken, viz. rapid removal to hospital, observation of contacts, delousing, and disinfection, the epidemic speedily declined in March. In the first week of April there were only three cases, and in the second week only one, the last. Of 194 cases admitted into two large school buildings which had rapidly been converted into hospitals, 141 were found to be suffering from typhus, and the remaining 53 from a variety of diseases, 21 of which were cases of typhoid, an epidemic of which was prevalent at the same time. Of 130 cases admitted during the febrile period 29 died, a mortality of 22 per cent. In 20 of these death took place during the acute stage, 2 died of pre-existing diseases (chronic bronchitis and tuberculosis) and 7 of complications (pneumonia, nephritis and haematemesis). The comparative mildness of the disease in early life and its severity in later years are shown by the fact that of 77 cases under 30, only 4 died, a mortality of 5 per cent., while between 30 and 40 the mortality was 18 per cent.; between 40 and 50, 43 per cent.; between 50 and 60, 70 per cent.; and between 60 and 70, 60 per cent. The mortality in the two sexes above 30 showed a distinct difference, about one-third of the cases in women being fatal as compared with one-half of the cases in men.

According to Pulido, three important outbreaks of typhus have recently occurred in Spain. The first, consisting of about 50 cases, occurred in the province of Burgos in June 1918, the second in the province of Murcia in January to May 1919, and the third outbreak, in which there were over 1,500 cases, in the provinces of Almeria and Granada in July 1919. This last epidemic was remarkably mild, for with the exception of two districts in which it was 50 per cent., the mortality did not amount to 4 per cent.

Jorge states that though typhus is endemic in Portugal, no important outbreaks had occurred until the endemic of 1918–19 in Oporto and the north of Portugal, only sporadic cases or localized epidemics having occurred since the Peninsular War, when typhus caused more deaths than Napoleon's army among the British expeditionary force. From the onset of the endemic at Oporto, in December 1917, to the end of December 1918, 6,254 cases of typhus were notified at Oporto with 1,203 deaths, a mortality of 19·2 per cent., and from January to the end of August 1919 there were 2,781 cases with 278 deaths, a mortality of 9·7 per cent.

Schweinburg records an epidemic of over 800 cases of typhus which occurred among German prisoners in Orenburg (Russia) in December 1915. The epidemic was a mild one and complications were rare. No case of gangrene occurred. The mortality was about 7 per cent. Schweinburg kept himself, his wife, and two soldiers who were in constant contact with the patients free from lice by soaking their under-linen twice daily in petroleum.

Zlocisti, who was in charge of the German Red Cross Hospital at Constantinople, states that of 1,716 typhus patients admitted between May 1916 and June 1918, 310 died—a mortality of 18·07 per cent., which closely corresponds to the figure given by Murchison of 18·78 per cent. No deaths occurred in the August of 1916 or 1917, the decline of the disease in the summer being due to increase in individual hygiene and the injurious effect on the lice of light, heat, and the damp skin of the sweating man. Age was the most important factor in the prognosis. Among children the mortality was almost nil, while in old age it was nearly 100 per cent., and between those two extremes there was a regularly rising curve. Race was of importance as regards the mortality only in so far as alcohol was concerned. The lower mortality among the Jews was due to their temperate habits.

Clemow states that typhus was rarely seen in Turkey before the war, and in Constantinople it was scarcely known as an indigenous disorder. Since the outbreak of the war, however, it has become widely epidemic throughout the greater part of the country. As regards its recent prevalence, the disease became epidemic in February, March, and April 1920 in Constantinople mainly as the result of the influx of Russian refugees after the defeat of Denikin's army. The highest number of cases in any one week (that ending March 13) was 78. In the summer the epidemic greatly declined, but the disease never wholly disappeared, and in the winter it became active again with the arrival of a still larger crowd of refugees from the Crimea after the collapse of Wrangel's army. Clemow estimates that the total number of known cases of typhus during 1920 was between 600 and 700.

An outbreak of eight cases of mild typhus in a home for foreign workmen at Paris is reported by Legry, Courcoux, and Lermoyez. Two cases from the same source, one of which recovered and the other died, are also reported by Labbé and Hutinel. The disease was at first mistaken for influenza, and it was not until the Weil-Felix reaction was performed at the Pasteur Institute that the correct diagnosis was established.

At a meeting of the Société médicale des hôpitaux de Paris on June 11, Netter and Salanier reported an isolated case of typhus in a lady, aged 28, which had been contracted at Cracow in Poland, showing that the disease does not spread in families where cleanliness is observed. The disease is transmitted by lice only, and owing to her having changed her under-linen several times in the course of her journey from Cracow to Paris, the patient had not brought any lice with her. In the subsequent discussion Renault stated that he had seen three simultaneous cases of typhus, in a camp of Polish workmen near Arras, who had contracted the disease before leaving Poland.

A proof of the important and perhaps exclusive rôle played by lice in the transmission of the disease is also given by Kramer (2) in his account of the epidemic at Amsterdam. The sanitary employees who were engaged in the transport of the patients and the disinfection of houses were required to keep their hair and beard closely shaved, to wear special clothes when on duty, and at the end of their day's work to return home in their own clothes. After this regulation had been made, eight employees contracted typhus, but although they remained at home some days before removal to hospital, no case broke out in their families.

**Symptomatology.** Löwy contests the truth of Jürgens's dictum that one case of typhus is just the same as another (vide *Medical Supplement*, 1918, **1**, 90), since typhus without eruption, attacks with a rudimentary rash, and those with a severe haemorrhagic eruption represent clinically distinct types of the disease. He records three cases of atypical typhus in children aged 5, 8, and 10 years respectively, in whom the fever lasted only five to seven days and was accompanied by very little general disturbance. In spite of the most careful examination no rash could be detected, but the diagnosis of typhus was established by the Weil-Felix reaction, which was positive in 1 : 200–1 : 1,600, as well as by the existence of an epidemic.

At a meeting of the Bucharest Medical Society, Constantinesco and Sloboziano reported two cases of **typhus without eruption** in which the clinical diagnosis was confirmed by the Weil-Felix reaction, which was positive in a dilution of 1 : 1,600. In the subsequent discussion Daniélopolu stated that he had never met with an example of typhus without eruption among a thousand cases of the disease, and Vignal declared that one should be very careful in making such a diagnosis. It was better to say 'without perceptible eruption'. In some cases the rash was very faint and transient. Sometimes, as in typhoid fever, it could only be seen in the scapulo-vertebral region. Moreover, in subjects with a pigmented skin like the Tziganes in Roumania, it might not be visible to the naked eye, but could be detected by examining the skin through blue glasses, when the eruption appeared in the form of black spots.

According to Kramer (2) widely divergent figures are given by different writers as to the duration of the **incubation period** in typhus. It is generally supposed to be from 9–12 days. The period may, however, be shorter, as was shown by the case of a nursing sister who went to Urk in September 1918 to nurse typhus, and on the eighth day after her arrival was severely ill with the disease. At the beginning of the epidemic at Rotterdam in 1918–19, contacts were isolated for 14 days, but subsequently this period was prolonged to 18 days, because in the second half of February two or three days after release from quarantine, two cases broke out in one family. The garrison at Rotterdam was isolated for 21 days, but as a rule isolation of contacts for 18 days, reckoning from the day of delousing is sufficient.

Gane describes a case of **relapse** in a man aged 21, who had a mild attack of typhus followed by a similar attack five days after the temperature had become normal. The eruption was typical of typhus in both attacks.

The diagnosis of enteric and relapsing fever was excluded in both attacks by examination of the blood.

Cantacuzène also reports a case of relapse in which there was an interval of 3½ months between each attack. In both cases the attack was of moderate intensity and uncomplicated, the second attack being an exact repetition of the first.

Dumitresco-Mante. of Bucharest, describes the following three forms of **pulmonary congestion** in typhus: (1) simple congestion, (2) perituberculous congestion, (3) pseudo-tuberculous or pseudo-phymic congestion. In the last form the congestion is localized at the apex, and presents the clinical and radioscopic appearances of pulmonary tuberculosis, but repeated examination of the sputum shows an absence of tubercle bacilli. The general condition is usually good, and complete recovery takes place in a few days or weeks. Although similar phenomena have been described in influenza and malaria, Dumitresco-Mante states that pseudo-tuberculous congestion which he observed in 10 out of 254 cases, has not previously been described in typhus. One of the factors of this congestion is the intense vasodilatation which occurs in typhus. The localization at the apex is difficult to explain and may possibly be due to a latent tuberculous focus. It must, however, be definitely distinguished from the congestion which occurs round a focus of active tuberculosis, and in most cases has a grave and progressive evolution.

Ströe examined the **cerebrospinal fluid** in 15 cases of severe typhus, all of which ended fatally, and found the streptococcus present in each case. In 12 of these it was also present in the blood. Ströe considers that the presence of this organism in the cerebrospinal fluid was due to septicaemia. Its absence in 3 cases does not negative this hypothesis, as a single blood-culture does not possess an absolute value. All the fluids were examined cytologically and showed the changes described by Daniélopolu (vide *Medical Supplement*, 1918, **1**, 91), Devaux (*ibid.*, 385), and others, the presence of the streptococcus in no way affecting the cell count.

Cantacuzène states that the general physiognomy of the Roumanian epidemic of 1917–18 was entirely different from that of the Serbian epidemic of 1915, which was characterized by the enormous proportion of cases of dry gangrene. In the Roumanian epidemic, cases of gangrene were extremely rare and did not amount to more than one case in a thousand. In the few cases which did occur the lower extremities only were affected, and the extensive areas of gangrene, involving the whole of the abdominal wall, such as were seen in the Serbian epidemic, were not observed. On the other hand the Roumanian epidemic was characterized by a **bulbo-pontine syndrome** of which hiccough, dysphagia, dyspnoea, and trismus were the principal features, some cases closely resembling rabies and tetanus.

Pfeiffer records a case of typical right **hemiplegia** and aphasia in a woman aged 26, which occurred on the first day after the temperature had become normal. Some improvement took place in the course of the next few months, but slight contracture of the elbow and wrist developed. Pfeiffer attributes the complication to a large embolic or thrombotic focus in the region of the left middle cerebral artery.

Moszeik reports a case of **lethargic encephalitis** following typhus, in a girl aged 18, to show that this syndrome may follow other infectious disease than influenza.

Grossfeld deals with the **onychodystrophy** of the fingers and toes following typhus which was described by Vogel in 1870 and by Murchison in 1873, and consisting in a groove 2–3 mm. broad running across the nail. It appears in the second month of convalescence and reaches the free border of the nail at about the sixth month. In several cases the retrospective diagnosis of typhus was made in convalescents who had had no history of illness.

The **aural and laryngeal complications** of typhus are discussed by Costiniu, of the Otorhinolaryngological Clinic of Bucharest, who states that during the Roumanian epidemic of 1917–18 nearly 70 per cent. of the patients had aural complications. In the early stage of the disease the middle ear only was affected, but in 10 per cent. the internal ear was also involved later. Recovery from otitis media was almost the rule, but recurrences were not infrequent. In otitis interna the results were less favourable. Improvement was obtained but was less lasting. Laryngeal complications, which were observed in about 15 per cent. of the cases, usually developed in convalescence. Diphtheria without concomitant faucial involvement was frequent. The evolution of these cases was unfavourable because the patient was unable to dispense with the tracheotomy tube. Costiniu therefore recommends that tracheotomy should only be performed in severe cases and never at the onset. Naso-bucco-pharyngeal antisepsis, when carried out from the first, definitely reduced the incidence of both aural and laryngeal complications and rendered them less severe when they did occur.

According to Vaudremer, **hypopyon** is a relatively frequent complication, as he found it in 12·8 per cent. of the cases of typhus in Epirus. As a rule it appears at the height of the disease and only in severe attacks, but sometimes it is delayed until convalescence. Its appearance is announced by violent pain in the eyeball and frontal and periorbital regions corresponding to the eye affected. When it develops in patients who are not moribund, it should be treated without delay, as recovery takes place without loss of the eye if an operation is performed at once.

Strominger, of Bucharest, when in charge of a urological section in a Roumanian military hospital, observed a large number of patients suffering from **cystitis** which had developed from six weeks to two or three months after an attack of typhus or relapsing fever. In some cases slight symptoms had been present during the fever and after a period of remission had become aggravated. Examination of the urine showed that the cystitis was not caused by exogenous infection except in one case where the presence of streptococci was due to frequent catheterization. In addition to the absence of micro-organisms and inflammatory symptoms, the late appearance of a complication like gangrene of the extremities and genitals is in favour of an exclusively toxic origin. The prognosis as a rule is good, but may be serious and even fatal when there are extensive renal and vascular lesions.

**Blood.** According to Cazeneuve, who examined the blood in 13 cases, typhus causes considerable changes in the leucocytes, viz. a variable but constant hyperleucocytosis, a pronounced neutrophil polynucleosis, eosinophilia, and a definite myelocythaemia.

Cantacuzène states that **association with other diseases**, especially cholera and relapsing fever, was characteristic of the Roumanian epidemic. All the cases of typhus in which cholera supervened were rapidly fatal, but relapsing fever did not appear to have any effect on the course of typhus or to aggravate the prognosis. Cantacuzène also refers to the action of typhus or latent tuberculosis. Without having the fulminating effect of relapsing fever, it is certain that in a very large number of cases of typhus, in which before the attack no appreciable evidence of lung disease was present, tuberculosis subsequently developed with great rapidity.

Glatard (1) records an epidemic of 206 cases of typhus at Oran in Algeria with 47 deaths—a mortality of 22 per cent. The incubation period varied from four to twelve days. Conjunctival infection was an early and very constant sign, being present in cases in which the eruption did not appear till late or was absent altogether. As regards the character of the eruption. petechiae were frequently absent, the typical lesion being a macule, which was at first pink and then became darker, and did not fade on pressure. The duration of the disease ranged from 16 to 18 days. In fatal cases death occurred either at the height of the disease from myocardial, pulmonary, or meningeal complications, or during its decline from collapse or nervous complications such as bulbar palsy or encephalitis.

**Diagnosis.** Lapin and Senevet, of the Pasteur Institute of Algiers, examined the Weil-Felix reaction in 158 cases of clinical typhus, and 20 controls with the following results: (1) None of the controls gave a positive reaction even in a dilution of 1 : 50; (2) of the 158 clinical cases 145 gave a positive reaction at least once, and of the 13 negative cases 5 had the reaction performed only once, 4 died before the end of the febrile period, and 4 were persistently negative. The agglutinating power of the cerebrospinal fluid was found to be very feeble. In 4 patients in whom the serum agglutinated Proteus X 19 at 1:500, the cerebrospinal fluid caused no agglutination at 1 : 50. In one patient in whom the serum agglutinated at 1 : 2,000, the cerebrospinal fluid agglutinated feebly at 1 : 50, and in another patient in whom the serum agglutinated at 1 : 3,000, the cerebrospinal fluid agglutinated at 1 : 100. The writers conclude that the Weil-Felix reaction is of great value in the diagnosis of typhus when it is positive, but as it only becomes positive towards the end of the disease no account should be taken of a negative reaction when the clinical symptoms justify the diagnosis.

Van der Reis records a case admitted to hospital as influenza in which the diagnosis of typhus was established by the skin reaction described by Friedberger and himself seven days before the Weil-Felix reaction became positive (vide *Medical Science* 1920, **1**, 563–4).

**Prophylaxis.** In a paper discussing the principles of prophylaxis of typhus in armies on active service, and their application to the civilian population in peace time, Armand-Delille describes Sarrailhé's method, which was systematically employed in the French army of the east during the Macedonian campaign. The clothes were ironed on their inner surface and especially along the lining. Although a single ironing did not destroy the lice and their ova, when the ironing was performed every seven days it was equivalent to a process of tyndallization, and it was absolutely efficacious if repeated for several weeks in succession. A generation of lice requires several days after hatching to furnish insects capable of reproduction. If therefore most of the lice and their ova are destroyed every seven days, in four or five weeks the evolution of the generations will be completely destroyed, as Sarrailhé and Récamier showed in a colonial regiment on the Albanian front.

Nicolle and Conseil have found that the serum of typhus convalescents and of monkeys who have recovered from the experimental disease possesses definite preventive properties. The immunity conferred, however, is only of short duration and the convalescent's serum is only active when it has been obtained during the first few days after the temperature has become normal. During a recent outbreak of typhus at Tunis, the writers employed the method in 7 cases, and none of the persons so treated contracted the disease. 4 were given a single injection of 20 c.c. and 3 two injections with a few days' interval between each.

According to Hunter the suddenness of the onset of the Serbian epidemic, dating from a particular day, was directly related to measures for stopping movements of people, and its recurrence, also dating from a particular day, was directly related to the resumption of such movements. The measures for checking the epidemic were the temporary cessation of railway traffic, suspension of leave from the army, and the improvisation of a method of disinfection which could be at the disposal of every one, especially the provision of 'barrel disinfectors'.

**Treatment.** According to Vaudremer, the treatment of typhus, which should be commenced as soon as possible, should be conducted on the following lines: (1) intramuscular injections of camphor oil (1 in 10) in doses of 2 c.c. every two hours if necessary; (2) injections of equal parts of camphor oil and ether in cases of profound asthenia and cardiac insufficiency; (3) digitalis by mouth or subcutaneous injections of digitalin systematically from the onset; (4) adrenalin by mouth or subcutaneously in doses of 1–2 mg. daily during the febrile stage, and later in cases of hypotension; (5) hydrotherapy should be forbidden, bad results being obtained owing to the profound asthenia and myocardial weakness.

Zielinski, of Warsaw, has treated 232 cases of typhus by hypodermic or intravenous injections of the patient's cerebrospinal fluid (vide *Medical Supplement* 1918, **1**, 176). He considers that this treatment should be employed in every severe case, especially when dangerous symptoms arise involving the nervous and circulatory system. The amount of fluid withdrawn should not exceed 20 c.c. and of that injected 10 c.c. If a re-injection is required, 3–5 c.c. may be given two or three days after the first injection. The cerebrospinal fluid obtained by lumbar puncture loses its activity at the end of a fortnight. The most favourable time to give the injection is from the 7th–10th day of disease, but in cases in which severe symptoms appear sooner, the injection can be given before the 7th day. Zielinski states that the method has yielded excellent results, the mortality among typhus cases so treated having fallen from 9 to 5 per cent.

Glatard (2) has treated 114 cases of typhus by intravenous injections of urotropin. The doses given at first were 1·50 gm. for adults and 0·75 gm. for children, but were afterwards raised to 3 gm. daily. The number of injections given varied from one to eight, the average being three. The results were as follows: (1) in the great majority of cases urotropin given intravenously favours defervescence, which occurs as a rule after the second injection; (2) it causes abundant diuresis, and therefore facilitates elimination of toxins; (3) it lowers the mortality, which was 14 per cent. among cases treated by urotropin as compared with 29 per cent. among cases not so treated; (4) it should not be used after the temperature has fallen, the myocardial asthenia being more suitably treated by camphor oil, strychnin, and nucleinate of soda injections.

Kersten states that intravenous injections of collargol or 'fulmargin', a finely colloidal silver preparation obtained by electrolysis, has a favourable influence on the course of the disease. 5 c.c. of a 5 per cent. solution of collargol can be given daily for eight days, or an ampoule of 'fulmargin' daily for seven days.

Monziols and Collignon treated 13 cases of typhus with an iodized Proteus X 19 vaccine containing 1,000,000,000 organisms per c.c. in doses ranging from 1–3 c.c. with the following results. The typhoid state diminished, the tongue became moist, the delirium subsided, the temperature and pulse ran a parallel course after the second injection, and the duration of the disease appeared to be shortened. The average number of injections given to each patient was seven. One death occurred among 13 treated with vaccine as compared with two among 13 not so treated.

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## WHOOPING-COUGH

**Aetiology.** Apert and Cambessédès draw attention to the fact that both in France and abroad whooping-cough shows a marked predominance among the female sex. Thus, during the year 1919 150 girls were admitted to the whooping-cough pavilion at the Hôpital des Enfants Malades, as compared with 88 boys. The statistics for the city of Paris from 1894 to 1903 also show a higher whooping-cough incidence and mortality among girls than among boys, though not so pronounced as that found by the writers at their hospital. The predilection of whooping-cough for the female sex is all the more remarkable as all the other infectious diseases of childhood, especially measles, scarlet fever, mumps, and diphtheria, are more frequent and severe in the male sex.

**Epidemiology.** Reiche (1), of the Hamburg-Barmbeck Hospital, states that, according to official statistics, of the four children's diseases, measles, scarlet fever, diphtheria, and whooping-cough, the last has the lowest morbidity but the highest mortality. In the period 1872–1912 the medical statistics of the Hamburg State show that there were 60,253 cases with 7,355 deaths, or a mortality of 12·2 per cent. This figure, Reiche admits, has only a relative value, as by no means all cases of whooping-cough, especially those of a mild character, were notified. It illustrates, however, the heavy mortality associated with the disease, the mortality being particularly high in hospitals where it is mainly the serious cases that are admitted. As in the other diseases of children, the mortality from whooping-cough is highest in early life and diminishes as age advances. Thus Hagenbach estimates that the mortality is 26·8 per cent. in the first year of life, 13·8 per cent. in the second year, and 3 per cent. in the third year. Of 66 deaths from pertussis under six years of age, which occurred in Reiche's whooping-cough department between April 1, 1914, and August 1, 1920, 16 cases were due to tuberculosis which had been lighted up by whooping-cough, and a quarter of these were caused by the miliary form. Another quarter of the deaths was due to a severe secondary infection, such as influenza, diphtheria, and lobar pneumonia, while two cases of infective meningitis were caused by haemolytic streptococci rather than by the causal agent of pertussis. It was thus clear that over a third of the deaths in Reiche's cases were not due to whooping-cough, while in another 14 per cent. of the cases severe rickets or the lymphatic diathesis was a favouring cause of death.

**Symptomatology.** Nasso records a case of whooping-cough in an infant aged 14 months in whom the paroxysms were accompanied or sometimes replaced by attacks of spasmodic sneezing. Death took place one morning during an unusually violent attack, being probably due to spasm of the glottis and cardiac syncope associated with spasmophilia. Nasso recommends that all cases of whooping-cough in infancy should undergo antispasmodic treatment even if there are no signs of spasmophilia present. In some cases subcutaneous injections of magnesium sulphate should be given.

According to Reiche (2), little is known of the association of whooping-cough and influenza. He reports an outbreak of influenza which occurred in his whooping-cough ward during the epidemic of influenza in January 1920. Of 16 cases in the ward 8 contracted influenza in the course of a few days, and shortly afterwards a child was admitted with both diseases, and died three days later. The mortality among the nine cases was very heavy, as six were fatal. In three of the cases there was a slight leucocytosis (14,800–16,400); in the cases of early double infection there was the excessively high leucocytosis of 172,000 per c.mm., while in four children the number of leucocytes fell to 6,400, and even 3,000. The lymphocytosis characteristic of whooping-cough was rapidly replaced by a predominance of the neutrophils on the supervention of influenza. With possibly one exception the course of influenza in these cases was less a toxic than a pneumonic one. At the autopsy there was a marked dilatation of the left ventricle resembling that seen in diphtheria. In one case which proved fatal in three days encephalitis was found *post mortem*—a complication liable to occur in both whooping-cough and influenza.

Reiche (3), in the course of 62 months, has seen 29 cases of whooping-cough complicated by convulsions. With 3 exceptions, aged 2, 3, and 4 years respectively, all the patients were infants in the first two years of life. 1 case showed tuberculous meningitis; 3 bacterial infection of the meninges due to streptococci, staphylococci, and pneumococci respectively; 1 thrombosis of the meningeal veins; and 6 other complications. The remaining 17 were examples of pure whooping-cough convulsions. The spinal fluid in each case was sterile, but showed an abundance of cells. There was a well-marked lymphocytosis in the blood. Reiche considers that convulsions are due to a serous whooping-cough meningitis.

Genoese examined the cerebrospinal fluid of six whooping-cough patients, aged from 2½–6 years, with the following results: In every case it was perfectly clear, under increased pressure, with a normal albumin and chloride content and without a fibrinous reticulum. There was an absence of acetone, Boveri's reaction was negative, and there was no increase in the number of cells. There was considerable increase of reducing substances, which was probably mainly due to meningeal congestion caused by the violent and repeated attacks of coughing. Experimentally, this hypothesis is confirmed by the fact that after spinal anaesthesia with stovain or cocain there is an increase in the sugar in the cerebrospinal fluid without hyperglycaemia. In such cases there is a marked congestion from local irritation without inflammation, just as in whooping-cough, in which there is a disturbance of the cerebral circulation and subsequent stasis.

Hess, of the Frankfort University Children's Clinic, came to the following conclusions from examination of the blood in whooping-cough patients: Lymphocytosis in whooping-cough is essentially caused by the paroxysms. Each attack produces a distinct increase in the total number of leucocytes with predominance of the lymphocytes. When there is a long interval between the attacks, the increase sometimes ceases, but normal values are not observed, both leucocytosis as a whole and relative lymphocytosis persisting. Very high values are found in the paroxysmal stage, and the highest of all during convulsions. Hess attributes the lymphocytosis to the pressure exercised by the abdominal and respiratory muscles on the spleen and thoracic duct, which are the 'central depôts' for lymphocytes.

**Treatment.** Intramuscular injection of ether in the treatment of whooping-cough is advocated by Audrain of Caen; Weill and Dufourt and Gleyvod of Lyons; and Cheinisse of Paris. The injections are given in the upper part of the buttock. The dose is 1 c.c. up to the age of 7 or 8 months, and in older children 2 c.c., repeated every two days. According to Weill and Dufourt, who regard injection of ether as far superior to any other treatment of pertussis, the ether acts in two ways, (1) by reducing the number of daily paroxysms, (2) by attenuating their violence and shortening their duration. In a few days' time, as the result of a daily injection, the children have only abortive attacks not accompanied by vomiting. It is unnecessary to continue the treatment when there are not more than four or five paroxysms a day.

Gleyvod, who reports eight cases in children aged from 2½ months to 8 years treated by this method in Weill's clinic, states that the first injections always have a more striking effect than the subsequent ones, the organism apparently becoming habituated to the ether. He maintains that there is no contra-indication to the use of ether when employed in doses of 1 or 2 c.c., and that it acts as an energetic cardiac stimulant in febrile forms of whooping-cough and those associated with much general disturbance and severe pulmonary complications.

From its use in 115 cases the vast majority of which were in children aged from a few weeks to 14 years, Macht has found that the administration of benzyl benzoate solution, either alone or preferably with small doses of benzaldehyde had a palliative, though not curative, effect on the violence and number of the whooping-cough paroxysms. 5–40 drops of a 20 per cent. solution of benzyl benzoate were given three or four times a day and oftener, according to the age of the patient and severity of the disease. The beneficial action of the drug is attributed by Macht to (1) its antispasmodic effect on bronchial spasm, (2) its sedative effect on skeletal muscle, (3) its anaesthetic effect on the larynx, (4) its expectorant properties, (5) its antiseptic action.

McMurray also claims to have obtained immediate improvement in cases of whooping-cough by the use of benzyl benzoate in doses of 5–30 minims every four hours without any undesirable results.

Lederer has treated 25 cases of pertussis by painting the throat every two days with a 2 per cent. solution of silver nitrate as recommended by Ochsenius. In the great majority of cases good results were obtained, the paroxysmal stage being considerably shortened, the frequency of nocturnal attacks diminished and long-standing attacks rapidly cured. Lederer attributes the success of the treatment to suggestion and not to a specific bactericidal action, and recommends that the method should be reserved for older children of a neuropathic disposition in whom the attacks have lasted a considerable time but without any complications. In such cases the treatment may produce an immediate cure.

Kleinschmidt has recently employed diathermy in a large number of cases of whooping-cough, and claims to have considerably shortened the duration of the disease thereby. The patient's age was of no importance, the youngest child being only nine months old, so that there could be no question of suggestion accounting for the success of the treatment.

Although vaccines for the prevention or cure of whooping-cough have been in use for the past eight years, Freeman has, until lately, been of opinion that they did not modify the course of the disease, and he had never seen a case prevented by their use. Recently, however, he has observed good results from the use of fresh vaccines in cases where vaccines three weeks old had no effect. The dosage used in his cases was half a billion for the first dose, one billion for the second dose, and two billion each for the third and fourth doses.

Spolverini reports the results of the prophylactic use of whooping-cough vaccine in 46 cases and of its curative use in 98 cases at the Paediatric Clinic at Rome. He found that prophylactic inoculation with a Bordet-Gengou vaccine, if carried out before the onset of the specific symptoms, gave excellent results, failures occurring in only 7 per cent. of the cases. Vaccine therapy was generally useless if employed 18–20 days after the onset, when typical paroxysms had already developed, and the Bordet-Gengou bacillus could no longer be found in the sputum. On the other hand, the treatment was successful if adopted within the first ten days of the disease, when the Bordet-Gengou bacillus could easily be found in the sputum. To ensure success larger doses were required, viz. two to four or even six thousand million per c.c., according to the age of the patient. The injections were repeated on alternate days. For prophylaxis three were usually sufficient, and for curative purposes six or seven were required.

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J. D. R.

## VACCINATION

Reece points out that during the five years 1913–17, the number of children vaccinated, as shown by the L.G.B. statistics, has continued to decrease and the number of children exempted by statutory declaration has continued to increase. The percentage vaccinated in 1917 was 43·3, and the percentage exempted 37·9, while 12·0 per cent. of the children born in that year were unaccounted for as regards vaccination. The circumstances of the war had the effect of increasing the number of persons who had been revaccinated, a very large proportion of the new army and a large proportion of the women auxiliary workers having been revaccinated. It is therefore certain that at the present time a greater number of the male population has been revaccinated than in previous years. Reece concludes that while the adult population is better protected against small-pox than previously, the proportion is unequally distributed between the two sexes, and that as regards the child population only about half the children under 10 years have been vaccinated.

According to the report of the chief medical officer of the Ministry of Health, after deducting 44,693 deaths which took place before vaccination among the 662,900 births reported by the several vaccination officers in England and Wales during 1918, it appears that of the surviving 618,207 children 44·5 per cent. were registered as successfully vaccinated, 0·2 per cent. as either insusceptible of vaccination or as having had small-pox, 1·9 per cent. as under medical certificate of postponement, and 40·3 per cent. with certificates of conscientious objection to vaccination, leaving 13·1 per cent. still unaccounted for as regards vaccination.

According to the vaccination returns for Bavaria for the year 1916, which are quoted by Soucek, among 12,018 primary vaccinations and 157,577 revaccinations there were no primary infections of the vaccination wound, and secondary complications occurred in only a very small number. All the cases with any complications recovered without any sequelae. During the first fortnight after vaccination a large number of cases of primary vaccination and a few revaccinated cases developed intercurrent diseases unconnected with vaccination, such as pneumonia, measles, diarrhoea, and vomiting, convulsions, and Werlhof's disease, which were the causes of death in 19 of the primary vaccination and 2 of the revaccination cases. The mortality among the primary vaccination cases in the first year of life was 3·9 per thousand, which was only a fraction of the mortality of the age-group to which the cases of primary vaccination belong.

Groth reports that in 1917 the results of vaccination in Bavaria were generally satisfactory. Of 116,171 children due to be vaccinated for the first time 92,765 or 79·85 per cent. were vaccinated and 23,406 or 20·15 per cent. remained unvaccinated, of whom 15,189 or 13·07 per cent. had a medical certificate to justify abstention. Public vaccinators vaccinated 86,269 successfully, 1,302 unsuccessfully, and 147 with unknown result, while private practitioners vaccinated 4,884 successfully, 160 unsuccessfully, and 3 with unknown results. In addition 4,387 were vaccinated during the first year of life, of whom 3,910 were vaccinated successfully, 188 unsuccessfully, and 13 with unknown results by the public vaccinators, and 259 successfully, 16 unsuccessfully, and 1 with unknown result by private practitioners. Out of a total, therefore, of 97,152 cases vaccinated for the first time, 90,179 or 98·20 per cent. were vaccinated successfully, 1,490 or 1·62 per cent. unsuccessfully, and 160 or 0·18 per cent. with unknown results by public vaccinators, and 5,143 or 96·62 per cent. successfully, 176 or 3·31 per cent. unsuccessfully, and 4 or 0·07 per cent. with unknown results by private practitioners. Of 161,176 children due to be revaccinated, 157,794 or 97·90 per cent. were vaccinated, 3,382 or 2·10 per cent. remained unvaccinated, of whom 2,178 or 1·35 per cent. had a medical certificate. 154,912 or 98·65 per cent. were vaccinated successfully, 1,818 or 1·16 per cent. unsuccessfully, and 295 or 0·19 per cent. with unknown results by public vaccinators, and 702 or 91·29 per cent. successfully, 65 or 8·45 per cent. unsuccessfully, and 2 or 0·26 per cent. with unknown results by private practitioners. 12 of the primary vaccination cases and one of the revaccination cases died. The causes of death in 5 cases was pneumonia, in 3 diarrhoea and vomiting, in 1 convulsions, in 1 diphtheria, and in 3, including the revaccination case, the cause of death was not stated. The mortality among the primary vaccination cases in the first year of life was only 3 per thousand.

Mensching states that owing to an outbreak of small-pox in Hamburg in the late autumn of 1916 due to Wolhynian refugees (vide *Medical Science*, 1920, **3**, 132), 684 new-born infants were vaccinated at the Hamburg Obstetrical Institute between December 18, 1916, and July 14, 1917. The vaccination was usually performed on the day of birth or the following day, but never later than the third day. In 484 or 71 per cent. it was successful and in 200 or 29 per cent. unsuccessful. The successful cases included 12 infants who had to be vaccinated twice. 18 infants failed to ‘take’ when the vaccination was repeated. The percentage of unsuccessful vaccinations was so high that it could not be attributed to deficient susceptibility to vaccinia or to the avirulent character of the lymph, but was due either to defective technique or to immunity acquired *in utero*. As a general rule the course of vaccination in the new-born showed no difference from that seen in older children vaccinated for the first time, typical vesicles occurring which reached their fullest development on the seventh to eighth day after vaccination. Severe constitutional disturbance hardly ever took place, though a loss of 50–100 grm. a day lasting for two or three days was frequently observed as the pocks reached their fullest development. In the great majority of cases vaccination had no effect on the temperature, fever, which is the rule in older children vaccinated for the first time, being quite exceptional. In 42 infants in whom fever did occur the phenomenon in most cases was due not to vaccination but to other factors. Among those vaccinated at the Institute were 82 premature infants, in 52 or 64 per cent. of whom the vaccination was successful, and in 30 or 36 per cent. unsuccessful, so that the percentage of unsuccessful vaccinations was 8 per cent. higher than in full-term infants. The local reaction was the same in the premature as in the full-term infants, and the general condition in almost all cases was not affected in any way.

As regards the vaccination state of the mothers, 281, with a single exception in which vaccination had taken place one year previously, had been vaccinated during pregnancy and usually in the last three months. 339 were vaccinated in the puerperium, in 6 vaccination was not performed, and in 58 no information was available. It was found that the number of unsuccessful vaccinations was larger among the children whose mothers had been vaccinated in pregnancy (Group I) than in those whose mothers had been vaccinated after delivery or not at all (Group II). 173 or 61·6 per cent. in Group I were successfully vaccinated, and 108 or 38·4 per cent. unsuccessfully vaccinated. In Group II, 261 or 75·6 per cent. of the vaccinations were successful and 84 or 24·3 per cent. unsuccessful. The percentage of unsuccessful vaccinations was therefore 14·1 per cent. higher in the children of the mothers vaccinated in pregnancy than in the others. Mensching considers it very probable that the failure of vaccination in these children is due to an immunity acquired *in utero*, especially as it was found that on repetition of vaccination and control tests defective technique or bad lymph was not responsible.

**Technique.** Goodall of Montreal recommends vaccination by subcutaneous injection, which he has carried out in approximately 6,000 men and a number of officers' children. From one-half to three-quarters of a tube of vaccine is used per individual. Sufficient sterile water is then added to make each injection equal to 1 c.c. The local reaction which usually occurs in two or three days' time resembles that following anti-typhoid inoculation, and is as variable in intensity. About 8 per cent. were negative. In 70 per cent. there was local swelling, heat, tenderness, slight pain and redness. In a small percentage of cases the reaction was very marked, causing swelling and oedema of the elbow, and in a few instances oedema of the whole hand and arm. In every case the local condition subsided without any signs beyond those of an intense local reaction. After the seventh to tenth day the local swelling and induration subsided, leaving a hard nodule in the subcutaneous tissue, usually ill-defined at first but becoming later well circumscribed and lasting for about a month. The advantages claimed for the method are as follows: (1) it is a clean surgical operation. If untoward results develop, they are due to faulty technique; (2) there is no open wound and dressings are therefore not required; (3) dangers of secondary infection are practically eliminated; (4) the percentage of positive reactions is very high; (5) in only a very small percentage did the local and general symptoms cause complete incapacity; (6) the method is painless as compared with scarification; (7) children undergo it without any difficulty, owing to the rapidity with which the injection is carried out.

During the last seven years, in which he has vaccinated over 500 children, Goldberger has used the inner and back side of the arm for vaccination for the following reasons: (1) it leaves no visible scar; (2) it does not prevent children having their daily bath while vaccination is going through its various stages; (3) there is little or no exposure to infection from outside sources of infection; (4) it minimizes the sources of trauma; (5) no infiltration, extensive induration, sloughing, or extensive scarring results. The method is as follows: after the arm has been cleansed the forearm is flexed at right angles to the arm, and the vaccine is applied below a line midway between the internal condyle of the humerus and the anterior axillary line. The virus is allowed to dry thoroughly before placing over the abrasion a sterile pad of gauze held in place by strips of adhesive plaster.

King believes that the balance of evidence is in favour of lanolized vaccine in respect to its resistance to tropical heat, and that as contrasted with glycerinated and desiccated vaccine the risk of injurious influence upon the virus is less. He gives the following comparative case success rates per cent., as found in Uganda, of different forms of vaccine in 1916: desiccated vaccine (Lister Institute, London) 66 per cent.; lanolized vaccine (Lister Institute, London) 91·32 per cent.; glycerinated vaccine (Nairobi) 67·32 per cent.; arm to arm 78·09 per cent.

**Complications.** From examination of thousands of persons who had been vaccinated or revaccinated, Gougerot has found that trichophytosis, although very rare, is the most frequent complication of vaccination. Trichophytosis, impetigo, and ecthyma, at the vaccination site were indeed the only skin eruptions of any frequency observed by him. Examples of ulcerative vaccinia, post-vaccinal eczema, psoriasis, and lichen were not seen. The individuals affected were of all ages, viz. soldiers, workwomen in powder factories, and children. The development of the lesions was usually slow. The following varieties were seen: (1) single and round; (2) small and oval; (3) circinate; (4) erythemato-squamous simulating psoriasis. The practical importance of these cases is that if their nature is not recognized they are improperly treated and do not heal.

At a recent meeting of the Section of Dermatology of the Royal Society of Medicine, Pernet reported a case of post-vaccinal psoriasis in a girl aged 16, in whom the eruption appeared two months after a primary vaccination, while the scabs were still present on the vaccinated areas. The lesions first appeared round the vaccination scars, and subsequently involved the elbows and extensor surface of the forearms, hands, and knees. There was no history of a rash before the vaccination. In the subsequent discussion Dore remarked that psoriasis sometimes occurred for the first time after slight injuries, and that this might possibly explain its occurrence after vaccination, and Fox reported the case of a medical man in Ceylon who had never had psoriasis before, but after revaccination developed psoriasis round the points of inoculation, the eruption subsequently spreading down the arm and eventually all over the body.

Wagner of Graz reports an unusual complication of vaccination in a woman aged 36, who was subject to hay fever, and had been unsuccessfully vaccinated two years previously. On appearance of the vaccine pocks she developed generalized oedema, asthmatic attacks, and a deposit on the tonsils. Albumin ($\frac{1}{4}$ per 1,000) was found in the urine. As the lesions on the arm subsided, all the other symptoms disappeared. Five other cases among 30 who were vaccinated at the same time developed tonsillitis, although there was no epidemic of sore throat prevalent. Deaths and severe illnesses following vaccination were also reported at the same time (July 1919).

Iyer records three cases of generalized vaccinia in Burmese children aged 2–3 years, from which it appears that the condition depends on personal idiosyncrasy, and not on climate, race, lymph, or the tube in which it is contained.

King alludes to the liability of native races to certain skin eruptions, and warns against hastily attributing their occurrence in the course of vaccination to the impurity of the vaccine employed. Thus, in parts of Africa during the hot season frequent instances of vesicular dermatitis and impetigo having no connexion with vaccination are normally found, and epidemics of 'pemphigus' are said to have occurred, though possibly such instances may have included the bullous form of impetigo contagiosa.

The development of phagedaena in the vaccine pustule towards the third or fourth day of its evolution is described by Blanchard, at Grand-

Bassam, Upper Guinea, who found a pure growth of the fuso-spirillar symbiosis on microscopical examination of the serum from the periphery of the lesions.

According to Naunyn, who has no doubt that there is a causal connexion between the two events, jaundice may occur in epidemic form in adults after revaccination. In such cases severe gastro-intestinal catarrh, shown by vomiting and diarrhoea, often lasts for weeks before the appearance of jaundice. The latter sets in suddenly, rapidly becomes intense, and lasts for more than six weeks. The liver is not enlarged and there is no fever. Bile-pigment is always found in the urine, but bile salts are not always present. Slowing of the pulse, pruritus and xanthopsia have been observed. The condition is never fatal. The most striking feature is the length of the incubation stage. In none of 199 cases recorded has the jaundice appeared earlier than two months after revaccination, and usually it has not developed till much later, even as long as eight months.

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## GONORRHOEA

**Aetiology.** The differences in *toxicity of different strains of gonococci* have been investigated by Jotten. By means of the methods of agglutination and complement fixation used to differentiate the several forms of meningococci, he was able to separate four groups of gonococci which he terms A, B, C, and D. The groups A and B were found to be more toxic for mice than groups C and D and the non-classified gonococci, and to possess greater resistance to the opsonic, bacteriotropic and bactericidal action of normal serum. It was also found that these groups were associated with severe and complicated cases of gonorrhoea in the human subject. No morphological or cultural differences between the more toxic and less toxic forms were discovered. Jotten remarks that these results show the importance of using autogenous vaccines, and explain the unsatisfactory results obtained by stock vaccines, which often do not contain the strain corresponding to that in the patient.

The two questions Lomholt has attempted to answer by a study of the 548 cases of recent venereal disease in men attending a free dispensary in the period October 1, 1916–May 1, 1920 are these: (1) What proportion of infections of men can be traced to professional prostitutes, i. e. women who receive cash down? (2) What proportion of infections occur under the influence of alcohol? Lomholt found his informants remarkably candid. Most of them (476) suffered from gonorrhoea, the short incubation period of which renders it more suitable for investigating these two problems than is the case with syphilis. In 153 cases, i. e. 28 per cent., infection was traced to professional prostitutes. As Lomholt points out, this ratio is much lower than Fournier has found to be the case in Paris or Blaschko in Berlin, the corresponding figures for these two towns being 72 per cent. and 81 per cent. respectively. Lomholt argues from his figures that brothel prostitution is dying out in Copenhagen, and is giving place to a less systematic and more human form of casual sexual intercourse. While only about one-quarter of all the cases of gonorrhoea and syphilis could be traced to professional prostitutes, they were responsible for half the cases of chancroid, the comparative frequency of which is greatest when the conditions of sexual intercourse are most degraded.

Of the 455 men questioned as to the influence, if any, of alcohol, 217 had taken the alcohol equivalent of two half-bottles of beer or more at the time of infection. In about three-quarters of these cases the men admitted to having been drunk. Thus, 48 per cent. contracted venereal disease under the influence of alcohol, and of the men infected by professional prostitutes, 75 per cent. were under the influence of alcohol. On the other hand, only 37 per cent. of the men infected by other than professional prostitutes had taken alcohol. The difference clearly shows that alcohol lowers the standard set by men in their choice of bed-fellows. In 72 cases, or 13 per cent. of the total, the men were married, and as many as 36, or 50 per cent., were infected by professional prostitutes. The proportion of drunkenness was also much greater among the married than the unmarried.

**Symptomatology.** A case of *gonococcal septicaemia,* in which the gonococcus was found in the blood and also in the sputum, is reported by Ribierre and Léobardy. The septicaemia developed a month after gonorrhoeal urethritis, which still persisted. A Gram-negative diplococcus was cultivated by the addition of 20 c.c. of blood, withdrawn during pyrexia, to a bouillon-ascites medium. Signs of pulmonary consolidation appeared at the right apex, with blood-stained expectoration. Examination of the sputum was negative for tubercle bacilli and for pneumococci, but positive for Gram-negative diplococci. As the pulmonary signs underwent resolution, and the diplococci were morphologically identical with gonococci, the authors conclude that the case was one of gonococcal septicaemia with a pulmonary metastatic complication.

A case of *gonococcal septicaemia complicated by icterus* is reported by Widal and May. As they remark, icterus may develop in the course of many infections, but is rare in gonorrhoea. The few cases hitherto recorded appear to have been all fatal. The case reported by these observers was severe, but was cured by five intravenous injections of antigonococcal serum, diluted 1 in 10. It is noted that beneficial effects with this serum have been obtained in gonorrhoeal arthritis, and the serum is recommended in all cases of general gonococcal infection, administered either intravenously or intramuscularly.

Jagic and Schiffner are of opinion that *gonococcal infection of the heart* is more frequent than generally supposed, and that if more attention was paid to the heart in cases of general gonococcal infection, more instances would be discovered, especially of the milder forms of myocarditis. They also think that gonorrhoea may account for some cases of myocarditis of obscure aetiology. They point out that endocarditis, which is the most common form of gonorrhoeal infection of the heart, may be vegetative or ulcerative. Vegetative endocarditis may be the only localization of general gonococcal infection, is more common than the ulcerative form, affects the mitral valves generally, and often leads to mitral insufficiency. The ulcerative form generally affects the aortic valves and runs the course of pyaemia. Myocarditis of gonorrhoeal origin, they remark, is not so well recognized. They distinguish two forms: (1) acute septic myocarditis, resulting in multiple abscesses in the myocardium, and generally resulting in pyaemia; (2) simple infective myocarditis. The latter, which is a rare condition, must be distinguished from functional cardiac symptoms of a vasomotor nature occurring during a period of pyrexia. Clinically, simple gonorrhoeal myocarditis is characterized by cardiac weakness, arhythmia, dilatation of the left ventricle, and mitral insufficiency. It may end in resolution or result in fibrosis. Two illustrative cases are given, both occurring in women, one complicating gonorrhoeal urethritis and arthritis, the other gonorrhoeal salpingitis. In both cases the cardiac signs appeared after resolution of the pyrexia and acute inflammatory local conditions, and in both there were signs of myocarditis with dilatation of the left ventricle.

While endocarditis is common in children in connexion with rheumatism and chorea, gonococcal endocarditis as a complication of vulvo-vaginitis appears to be rare. A case of *malignant endocarditis due to the gonococcus*, in a child aged 23 months, is reported by Dwyer. The symptoms included a vaginal discharge, pain and swelling of the left ankle and wrist, some degree of anaemia and jaundice, abdominal distension, and a temperature of 104° F. The cardiac signs consisted in a rapid and irregular pulse, and a soft, systolic murmur at the apex conducted to the axilla. There was also a superficial abscess over the lumbo-sacral region. Microscopic examination of the vaginal discharge showed Gram-negative intracellular diplococci. The same were found in the pus from the lumbo-sacral abscess. Blood culture on ascitic glucose broth and ascitic glucose agar resulted in a growth of the same diplococcus (gonococcus). The child died on the twenty-eighth day of her illness. The autopsy showed cauliflower vegetations on the mitral valve, in which gonococci were found. The other valves were normal, and there was no pericarditis. There was no evidence of peritonitis. The lumbo-sacral abscess was attributed to localization of gonococci from the blood-stream due to lowered resistance in the area from pressure, a condition analogous to a bed-sore. The case is of interest on account of the age of the patient, the cultivation of the gonococcus from the blood, and the rarity of gonococcal endocarditis in children. Satterthwaite is quoted as having found only one case in a hundred, and Dunn as having found none of gonococcal origin in 304 cases of endocarditis in children.

Strandberg and Hedenius report a case of chronic gonorrhoeal arthritis complicated by *keratodermia blenorrhagica.* The patient, a male aged 26, had three attacks of gonorrhoea in the course of four years. The first attack was complicated by arthritis of the knee, which recurred during the later attacks, and eventually affected the shoulders, wrists, and cervical vertebrae. The cutaneous lesions commenced six years after the first and two years after the last attack of gonorrhoea. They were situated on the lower part of the right leg and ankle, the upper part of the left leg and knee, and on the right hand. Microscopic examination showed changes similar in nature to those described in other cases of gonorrhoeal hyperkeratosis. The patient died from cachexia the following year.

The authors remark that keratodermia blenorrhagica occurs, as a rule, in cases of severe gonorrhoeal infection complicated by multiple arthritis, bad general condition, and cachexia. The cutaneous lesions generally affect the lower extremities, are of an inflammatory nature, and characterized by a predisposition to parakeratosis, manifested by the formation of thick, horny patches. In many cases there is also present a hyperkeratosic balanitis. Although the affection occurs in association with gonorrhoea, it may be partly due to secondary infection. The names keratodermia or hyperkeratosis are inexact, the lesions being more of the nature of a parakeratosis.

Adamson draws attention to the resemblance between this affection and arthropathic psoriasis of the palms and soles, and points out that in many cases of gonorrhoeal hyperkeratosis there are lesions of the trunk which are indistinguishable from psoriasis. He suggests that psoriasis may possibly be due to a microbe allied to the gonococcus.

**Diagnosis.** Magner reports his experience with the *complement-fixation test* in gonorrhoea. The technique employed was similar to Thomson's; the antigens tried were Thomson's and Parke Davis & Co.'s; the complement was obtained from guinea-pig serum; the haemolytic system consisted of haemolytic serum, prepared by Burroughs Wellcome & Co., and sheep's cells. The patients' serum was heated to 60° C. for ten minutes and then diluted. 200 cases were examined, 110 gonorrhoeal and 90 control. In the gonorrhoeal cases, the test was generally negative up to 10 or 12 days after infection, afterwards most cases were positive; but some mild cases in which the urethritis was limited to the anterior urethra were negative. The longer the duration of the discharge the more often is a positive result obtained. The complications of gonorrhoea, such as epididymitis and gonorrhoeal rheumatism, were always positive. A positive reaction was obtained for three months after gonococci were absent, so that the reaction is no test of cure till three months without treatment have elapsed since the last symptoms.

Magner regards the test as useful in the diagnosis of cases which are negative microscopically. A positive result shows either that gonococci are still present, or that the antibodies they give rise to are still present in the serum. A negative result, especially after a previously positive one, is strong evidence of a cure. The administration of an autogenous gonococcal vaccine did not appear to prolong the positive stage to any great extent. The control cases were all negative, except four, all of which were syphilitic. and so might have been infected with gonorrhoea as well.

The difficulty in diagnosing gonococcal infections by cultural methods, and the uncertainty of the complement-fixation test, led Robinson and Meader to apply a *precipitin test*, similar to that used in pneumococcus and meningococcus infections. For this purpose they tried the reaction of immune rabbit serum and the autolysate of gonococcus cultures. Their method is described as follows: Rabbits were injected intravenously with single strains of gonococci in gradually increasing doses at seven-day intervals. Five or six injections were generally sufficient to produce a serum giving a marked precipitin reaction in a dilution of 1 in 20. The autolysate was prepared by washing off the growth of gonococci on rabbit blood agar in 5 c.c. of normal saline solution and allowing it to stand in an incubator for six hours. This suspension was centrifuged, and the supernatant fluid superposed on an equal quantity of the immune serum. The tubes were then placed in a water bath at 37° C. for one hour. After cooling, the results were read. A positive reaction was indicated by a cloudy-white ring at the junction of serum and autolysate. All strains of gonococci gave a positive reaction with immune serum, and no differences were noted between homologous and heterologous autolysates, so that there appeared to be no strain specificity.

For purposes of diagnosis the autolysate is obtained by moistening a sterile swab in the material to be tested and incubating in 2 c.c. of normal saline solution for six hours. The swab is then removed and the infusion centrifuged. If, as occasionally happens, the fluid remains opalescent in spite of centrifugalization a correct reading can be obtained by comparing density of the precipitated ring with that of a control tube containing normal rabbit serum.

The procedure is described as follows: For each specimen to be examined 0·25 c.c. of diluted clear serum from two immune and one normal rabbit are placed in test-tubes. The clear extract of the specimen is superposed on an equal amount of serum. The tubes are incubated for one hour at 37° C. and allowed to cool. Two immune sera are used in order to duplicate the results, and the serum from a normal rabbit is used as control.

The authors found that some sera gave a false reaction when saline solution was added, but obviated this difficulty by diluting the serum with saline (one to two) and centrifuging till clear. From their researches, they conclude: (1) that a positive precipitin test is obtained in all cases where the gonococcus is found in the discharge; (2) that it is also obtained in many cases where the history and symptoms point to gonorrhoeal infection, but in which the gonococcus cannot be found in the secretion; (3) that the test is of value in the diagnosis of vaginal and other specimens where the microscopical demonstration of gonococci is difficult or impossible.

It is interesting to note that the meningococcus gave a positive reaction with gonococcus immune serum when a concentrated pure culture autolysate was used, but the gonococcus control autolysate continued to give a positive reaction for a considerable number of dilutions after the reaction with the meningococcus had become negative. *Micrococcus catarrhalis*, *B. coli*, and all other organisms tested gave negative reactions.

**Treatment.** Müller, having observed that concomitant gonorrhoea was improved in patients under treatment for sycosis by intramuscular injections of turpentine and 'aolan' (a trade name for a sterilized solution of milk albumin), tried the same treatment in cases of gonorrhoea. These substances are said to have a beneficial effect in staphylococcal infections. The conclusions arrived at were: that the duration of acute anterior urethritis was shortened to a period of three weeks; that acute posterior urethritis subsided after two or three injections, so that local treatment could be carried out; that chronic posterior urethritis was also benefited; that complications were less frequent, and that both drugs were useful in epididymitis. The dose of turpentine was from 0·5 to 1·0 c.c. given at intervals of three or four days; that of 'aolan' from 6 to 7 c.c. In cases of cystitis and pyelitis, Müller recommends intravenous injections of 0·15 to 0·30 grm. neosalvarsan, which he thinks acts by the formaldehyde contained in it.

The results of the treatment of gonorrhoeal arthritis by a non-specific protein (usually *Bacillus typhosus*) have led to further experimental injections. Stern and Ritter state they have found the intravenous injection of a solution of sodium iodide to produce undoubted benefit in cases of gonorrhoeal arthritis, epididymitis, and prostatitis. Both acute and chronic conditions are benefited. The results observed are claimed to be not less than those following the injection of a non-specific protein. The authors observe that the efficacy of the latter form of treatment appears to be dependent upon the production of leucocytosis and a marked febrile reaction. Sodium iodide produces no alteration in the blood-count, and no reaction effects at all; the injections may therefore be employed without hesitation in the treatment of out-patients and in the private consulting-room. The drug was administered in doses of 2 grm. dissolved in 20 c.c. of water, and the injections were repeated every four days. All the usual therapeutic measures were employed in conjunction with intravenous medication. One hundred cases have been discharged 'germ-free' and apparently cured; the authors estimate that the average stay in hospital of these patients has been reduced by one-third owing to this additional treatment.

**Gonorrhoea in the female.** In 3,439 examinations of prostitutes Stevens and Heppner found *chronic gonorrhoea* in 43·5 per cent. The cervix was affected in 47, the urethra in 32, and one or both Bartholin's glands in 23 per cent. of the cases. The complement-fixation test was positive in 59 per cent. of cases of cervical infection, in 23 per cent. of urethritis, and in 19 per cent. of bartholinitis. In the treatment of endocervicitis good results were obtained from the application of a 25 per cent. solution of silver nitrate twice weekly in conjunction with hot vaginal douches. Better results were obtained by cauterization of the cervix. In urethritis gonococci were found in about one-third of the cases; other organisms present in order of frequency were Gram-positive diplococci, staphylococci, streptococci, diplobacilli, and other bacilli. The importance of examining Skene's and other glands near the meatus, which are usually affected in gonorrhoeal urethritis, is pointed out. In the absence of complications acute urethritis in the female usually clears up with sandalwood oil, alkaline drugs, and rest in bed. Chronicity was generally due to glandular infection or stricture. Strictures at the meatus or within the urethra were found in 58 per cent. of the cases. The treatment adopted consisted in instillations of 1 to 3 per cent. solutions of silver nitrate, and application of stronger solutions through a short endoscopic tube. Acriflavin and mercurochrome proved of little value. Infected glands and ducts were destroyed by the cautery and strictures were dilated or incised. With regard to Bartholin's glands, the authors point out that a normal gland is usually impossible to palpate, and that a palpable gland generally means infection. Treatment by injection of various solutions proved of little or no value, and the authors recommend excision of the gland both in acute and chronic cases.

As Rawlins points out, in the treatment of gonorrhoea in women, the results will be disappointing if care is not taken that no infected part is overlooked, such as Bartholin's and Skene's ducts. Infection of these ducts is common and persistent, and also of the urethra. The ducts can be washed out with a syringe and blunt-pointed needle, and if this fails the duct can be incised and treated with iodized phenol or destroyed by the electric cautery. Urethritis usually clears up with local application of picric acid and internal urinary antiseptics. According to Rawlins, the most satisfactory drug for local treatment is 50 per cent. picric acid in glycerine, applied by swabbing to the vulva, vagina, and cervix two or three times a week. Sauerin pessaries were also found useful. Douching is not recommended unless the tubes are affected, when the warmth of the douche is beneficial. A douche at high pressure, performed by the patient herself, is considered liable to cause spreading of the disease to the uterus. If douching is done, the patient should lie on her back with the buttocks slightly raised, and the douche-can not more than 1½ feet above the level of the body.

Jacoby recommends the following treatment. During the acute stage of urethritis, rest in bed, hyoscyamus and sandalwood oil. After the acute urethritis has subsided, urethral injections of 1 per cent. protargol or 20 per cent. argyrol every other day. In chronic cases, instillation of ¼ per cent. protargol or 1 in 10,000 silver nitrate into the bladder three times a week; the application of 5 per cent. silver nitrate to ulcerated areas of the urethral mucous membrane through a speculum; injection of Skene's tubules with 10 per cent. silver nitrate daily, or, in obstinate cases, cauterization. Of the more recent remedies, 1 per cent. acriflavin or mercurochrome give promising results as a urethral injection. In acute endocervicitis, similar treatment to that for acute urethritis. In subacute and chronic endocervicitis, the application of 25 per cent. argyrol or 1 per cent. protargol to the cervical canal, followed by glycerine and packing the vagina with gauze three times a week. The packing is removed after 18 hours and followed by douches of permanganate of potash 1 to 5,000, tincture of iodine 1 to 500, acriflavin or mercurochrome 1 to 5,000. Gonococcal vaccine, 500 millions every five days is useful in chronic cases. In the treatment of complications conservatism is advised, operation being only resorted to when unavoidable.

Before a case is discharged as cured, Jacoby insists on the following conditions being fulfilled: (1) Smears from the cervix, urethra, Skene's and Bartholin's glands, some taken just before and some just after menstruation, should be negative on six occasions; (2) smears after provocative injection of the urethra should be negative; (3) the complement-fixation test should be negative; (4) all these tests should be negative when repeated a month after cessation of treatment.

Having previously obtained good results from the treatment of certain gonorrhoeal complications, such as arthritis and epididymitis, by *intravenous injections of arsenical compounds,* Lévy-Bing and Duroeux have tried this method of treatment in cases of acute *gonorrhoeal salpingitis,* with equally beneficial results. In these cases the arsenical preparation used was sulpharsenol, administered in doses of 0·06 up to 0·18 grm. at intervals of two or three days. In one case, where a woman was confined to bed with repeated metrorrhagia, high temperature, anaemia, and pain, the haemorrhages ceased, the pain subsided, and the patient was able to get up within a week after the first injection. Bimanual vaginal examination also showed subsidence of the pelvic inflammatory condition. Three cases of chronic relapsing salpingitis, treated in the same way, were also reported cured in a few weeks.

Dorland advocates the local application of *methylene blue,* 1 per cent., in the treatment of gonorrhoea in women. The advantages are said to be—powerful gonococcicidal action, absence of irritation, rapid relief of clinical symptoms, and disappearance of gonococci after six to twelve applications. According to Dorland, methylene blue, which was used some years ago in the treatment of gonorrhoea, was chiefly administered internally, and was abandoned because it appeared to undergo some change in the body which rendered it inert. As a local application, however, he considers it superior to those in general use.

Although the value of *serum treatment in gonorrhoea* has been questioned on the grounds that the gonotoxin is an endotoxin, and, therefore, to be attacked by vaccines instead of serums, several observers have reported good effects from the use of antigonococcal serum. Ivens has tried antigonococcal serum in 30 cases of gonorrhoea in women, in 22 of which tubal infection was present. The serum used was Nicolle's, prepared at the Pasteur Institute, and was administered in three different ways. In one series of cases the serum was injected subcutaneously, usually in doses of 20 c.c. diluted with normal saline, repeated at intervals of 2 to 3 days. In another series intraperitoneal injections were given. In cases of pyosalpinx the tube was washed out with normal saline, after being opened up if necessary. The serum was injected into the tubes, sometimes into the ovary, and the abdomen was then closed without drainage. A subcutaneous or rectal saline was given at the same time to avert anaphylactic shock. In a third series of cases of endocervicitis with profuse leucorrhoeal discharge the serum was used locally in the form of vaginal packs, alternating daily with packs of 10 per cent. saline solution and 5 per cent. carbolic acid. Intravenous injections of serum were not used, on account of the danger of anaphylactic shock. Of the 30 cases, subcutaneous injections were used in 19, intratubal and intraperitoneal in 6, vaginal packs in 3, and serum dressings in 2 cases of bartholinitis. In all the cases the immediate results were good, and the after-histories satisfactory in most cases. Three cases relapsed, one possibly owing to insufficient serum being used, the other two probably from reinfection. In the intraperitoneal cases the results were much better than in cases where no serum was given at operating, and in one case pregnancy was proceeding normally.

As Daken remarks, *gonorrhoeal vulvovaginitis* in children is obstinate, owing to the foci of the disease being difficult of access and to the frequency of involvement of the cervix. For this reason clinical symptoms may clear up under treatment and relapses occur subsequently. He mentions a case, a girl aged seven, in which the bacteriological examination became negative after treatment with urinary antiseptics, vaginal irrigations, protargol pessaries, sitz baths, and diathermy. After provocative injections of Lugol's solution and 'aolan' (milk albumin), however, gonococci were again found in the secretion. The case was eventually cured with vaccines (arthigon). As a test of cure, therefore, he recommends—after cessation of treatment and negative bacteriological examination for ten days—provocative injections of Lugol's solution and 'aolan', repeated after a week and again after two weeks. If still negative for gonococci after this procedure the case may be considered cured.

Patzschke recommends the addition of adrenalin hydrochloride to the silver solutions used for irrigation in the treatment of vulvovaginitis in children. By the action of the adrenalin on the hyperaemic mucous membrane it is claimed that stronger solutions of silver preparations can be used. The method of treatment is as follows: after cleansing the vulva, the vagina is injected with weak permanganate solution, which is retained for five minutes by closing the labia. A tampon soaked in 5 per cent. protargol solution is then placed in the vulva. Irrigations four times a day are then performed, commencing with 0·5 per cent. albargin solution, to which is added 1 in 1,000 adrenalin solution (0·5 to 2 in 20). After three or four days the strength of albargin is increased to 1 per cent., and in ten days up to 2 per cent. After a fortnight the irrigations are done once a day only, and a smear is tested for gonococci. If the result is negative the treatment is continued for another ten days. If again negative 24 hours after cessation of treatment, the irrigations are discontinued. In 11 cases treated in this way there were only two relapses.

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## CHANCROID

According to Cheinisse, chancroid and its complications are more common than is generally supposed. Out of a total of 235 primary sores observed at the General Hospital at Rouen, 61 were syphilitic, 125 chancroid, and 49 mixed; and out of a total of 155 primary sores observed at a military venereal centre 89 were syphilitic, 64 chancroid, and 32 mixed.

**Symptomatology.** That all genital sores diagnosed as *ulcus molle,* or chancroid, are due to the bacillus of Ducrey is doubted by McDonagh. He also casts doubt on the usually accepted doctrine that a chancroid frequently develops into a syphilitic chancre owing to double infection. In such cases he regards the initial diagnosis as incorrect.

The varieties of *ulcus molle* described by McDonagh are: (1) *ulcus molle elevatum,* in which the sore is raised and often indurated, rendering it liable to be mistaken for a syphilitic chancre; (2) *ulcus molle miliare,* resembling hair follicle infection and more common in women; (3) *ulcus molle phagedaenicum,* which he regards as less common than phagedaenic syphilitic chancre, and due to the symbiosis of fusiform bacilli and spirochaetes similar to those found in Vincent's angina and balanitis gangrenosa; (4) *ulcus molle serpiginosum.* This last variety he considers to be more common than generally supposed, and to be usually wrongly diagnosed. This variety resembles a furuncle, the edges of which become blue and break down into an ulcer. The base of the ulcer is uneven and secretes freely; the edges are ragged and undermined, the overhanging portions being oedematous and bluish-white in colour. The periphery of the lesion is of a purple colour and is surrounded by a red zone of inflammation. The ulcer spreads at one part while the opposite part is healing, and the lesion may gradually progress for years. In a case described by McDonagh the lesion spread from the groin up to the umbilicus and down to below the right knee in the course of 27 years. Ducrey's bacillus was found intracellularly in this case. Ulcus molle serpiginosum is thus a very chronic form of ulceration following a chancroid, and occurs chiefly among people who have lived in the tropics. In some cases it develops from a bubo after the original sore has healed.

**Diagnosis.** Teague and Deibert point out that the difficulty in diagnosing chancroid from microscopical examination of smears is due to the fact that the bacillus of Ducrey in passing from the tissues into the purulent discharge loses its characteristic arrangement in long chains and appears in the form of small pleomorphic bacilli, from which it is unsafe to make a definite diagnosis. They therefore tried the method of *culture*, from which they report successful results. The medium used for culture was rabbits' blood allowed to clot at room temperature, then heated for five minutes at 55° C, and either used at once or kept in the ice-chest overnight. Tubes of this medium were inoculated with pus from the sore to be examined, and after 24 hours' incubation at 37° C. the serum showed characteristic chains of the small Gram-negative bacillus of Ducrey, sometimes apparently in pure culture, sometimes mixed with Gram-positive cocci and bacilli. Positive results were often obtained after the application of antiseptic ointments, &c. Previous washing with sterile salt solution was found unnecessary. Human blood was tried for culture, but found inferior to rabbits' blood.

By this method, Teague and Deibert examined 274 sores situated on the penis. As they obtained a positive result in more than 50 per cent., and as most of the negative cases showed no clinical evidence of chancroid, they conclude that a diagnosis of chancroid can be made in probably over 90 per cent. of cases by the method of culture. They attribute the failure of the cultural method in other hands to the use of unsuitable media. The bacillus of Ducrey does not grow on any of the ordinary media except blood agar, and on this with difficulty.

**Treatment.** Cheinisse reviews the various methods of treatment which have been tried, including: (1) filiform drainage combined with dressings of permanganate of potassium 1 in 200; (2) incision, followed by the application of a Bier's cup for ten minutes, and then injections of iodoform emulsion; (3) Goubeau's method, by injection of a 1 per cent. solution of arseniate of sodium before softening has occurred. In this method, if suppuration has occurred, the pus is evacuated by a small trochar and 1 or 2 c.c of the arseniate solution mixed with 0·5 c.c. of ether is injected; the ether, becoming gaseous at body temperature, distends the abscess cavity and allows more complete contact with the solution. The injections, are made daily or every other day; (4) Lasserre's emulsion for injection, consisting of 10 parts each of iodoform, guaiacol, eucalyptol, and alcohol, 30 parts of balsam of Peru, and 100 parts of ether.

Cheinisse also mentions that a favourable influence on the evolution of chancroidal bubo was obtained by Kurita, a Japanese surgeon, by means of a vaccine prepared from the bacillus of Ducrey.

Reenstierna claims good results from the use of a serum obtained from rams after intravenous injections of killed and living cultures of Ducrey's bacillus. In 100 cases of chancroid with bubo the sores are said to have healed and the buboes to have subsided in a week, after two injections of 10 c.c. of this serum. It is also stated that the serum had no effect on cases wrongly diagnosed as chancroid.

McDonagh recommends cauterization by camphphenol or by zinc ionization, followed by the application of a dusting powder consisting of equal parts of bismuth subgallate, bismuth tribromphenolate and light magnesium carbonate, mixed with starch. In chronic sores he gives two intramuscular injections of intramine, followed by two intramuscular injections of 'trimine' (a colloidal mixture of manganese, iron, and zinc), also a local dressing of intramine. The sores should be exposed to the air and not covered with air-tight dressings. In cases of sores concealed by a tight prepuce the latter should be slit up, but no other operative measure should be carried out, as the wounds always become infected and phagedaena often results.

In the treatment of bubo, incision should be postponed as long as possible; many cases subside under evaporating lotions, such as a mixture of subacetate of lead, strong solution of ammonia, rectified spirit and acetate of alum. If an incision is necessary it should be a small one; a long incision leads to infection of the interglandular tissue, leaves a wound which takes a long time to heal, and may result in phagedaena. Puncture with a bistoury, expression of pus, washing out with saline solution, and dusting with the powder mentioned above are sufficient. According to McDonagh, buboes may be aborted or rapidly healed by intramuscular injections of 'trimine' and intramine. In cases of *ulcus molle serpiginosum* operative measures are contraindicated. McDonagh recommends colloidal iodine internally (three drachms thrice daily), and intravenously (100 c.c.) followed in two days by an intramuscular injection of intramine (3 c.c.), repeated five days later and followed by one to three injections of trimine or an antimony salt. Locally, camphphenol and iodoform or intramine. The chronic case of 27 years' duration already mentioned, which had resisted all the usual forms of treatment, is said to have healed under local applications of intramine, intravenous injections of tartar emetic and intramuscular injections of intramine.

Golay recommends Fontan's method of treating chancroidal buboes in suitable cases. This method consists in making a small puncture with a bistoury, evacuation of pus, injection of 10 per cent. iodoform vaseline, and sealing the puncture. After 48 hours the vaseline is evacuated. In favourable cases cure is said to take place in four or five days. According to Golay this method is successful under certain conditions which are briefly as follows: (1) The bubo must be completely softened. If there is a tendency for the pus to point before the gland has completely softened it is better to open freely and curette, because the method of Fontan will only express the pus of the periadenitis and leave that in the gland which will form a fistula afterwards. (2) There must be no involvement of the skin by the bacillus of Ducrey; this requires energetic cauterization. (3) There must be no burrowing of pus, as Fontan's method will not distend the pockets. (4) The essentials for success are complete expression of all pus and distension of the cavity with the same amount of iodoform vaseline as the pus evacuated. The vaseline should be heated and then cooled to the right consistency. The patient should remain in bed for 48 hours.

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## SURGICAL TREATMENT OF CHRONIC INTESTINAL STASIS

When surgical treatment is advocated for cases of constipation which have not been relieved by medical treatment it is objected that indications for the operation have not been clearly stated, that the results of operations have not been fully disclosed, and that there is a tendency to practice one and the same operation for a number of probably quite different cases.

For an advance on these questions the first thing to do is to sharply distinguish the cases of constipation which are caused by some form of mechanical obstruction. Such causes are multifarious, their number is being continually increased, and the particular form of operative treatment depends upon the special variety. Much more experience is needed before it can be stated that some one procedure is the best to be applied to any number of cases of obstruction.

The surgical treatment of intestinal stasis when there is no naked-eye mechanical cause of obstruction has its chief advocate in Arbuthnot Lane.

The fourth edition of his work *The Operative Treatment of Chronic Intestinal Stasis*, appeared in 1918, and was reviewed in the *British Journal of Surgery*. The concluding paragraph of that review is as follows: 'The opinions offered by Sir Arbuthnot Lane in support of his views lack adequate corroboration from his own work, or from that of any of the contributors to this volume. Where we look for reasoned argument we find wild assertion; we seek in vain for any record of mortality, or for any series of cases in which the previous history, the operative disclosures, the risk of operation, and the late conditions are set forth in a manner which allows a reader to form his own judgement. Our faith is tried to the breaking point.'

Hurst has dealt very fully with the subject of *Constipation and its*

*Treatment.* He commenced a chapter on 'Operative Treatment' as follows: 'When constipation is the result of definite organic obstruction of the intestine, surgical treatment is clearly indicated. But various operations have been recommended in the last ten years for the relief of constipation in the absence of this clear indication,' and he proceeds to refer unfavourably to the various measures.

Since the above, Lane has published remarks on intestinal stasis in which he has added to the list of causes and indications a great number of the most various conditions which, in his opinion, combine to make the colon the essential cause of intestinal stasis. His remedy is the excision of the gut from near the end of the ileum to the end of the pelvic colon or sigmoid flexure, and the end to end union between the ileum and the junction of the colon with the rectum. But these further communications do not supply what the above-mentioned review desired—information as to results.

Wide publicity was gained by Metchnikoff for such statements as 'It is not more rash to say that not only the caecal appendix with the caecum, but indeed the entire human large intestine is for our organism a superfluous organ, the suppression of which would have very happy results. From the point of view of the digestive function, this part of the intestinal tube certainly plays no, however small, important rôle.' If the chapter from which the above quotation is taken be re-read one can but form the opinion that Metchnikoff had reached his conclusion because the functions of the large intestine were unknown to him.

There is an important chapter in Lane's book contributed by Keith under the title 'The Great Bowel; from an Anatomist's Point of View'.

Keith noted the division between juice digestion in the small intestines, and the bacterial digestion in the large bowel, which is regulated by, and regurgitation prevented through, the mechanism of the ileo-caecal valve. The colon may become an injurious structure, but for the comparative anatomist the idea that nature has elaborated a great and persistent structure, such as the colon, for no definite and useful purpose is preposterous.

There is something to be said for the proposition that the colon remains more suited to digest the vegetarian diet of primitive man, and has not become sufficiently adapted to the concentrated food of modern town-dwellers. But a diet of coarse vegetables notoriously produces an excess of flatus which demands expulsion whether upward or downward.

The concentrated diet forced upon healthy young men under the exigencies of military service has set up much troublesome constipation. The service rations and the food substitutes in Germany have produced a marked increase of obstinate constipation, and this was the reason for a long address by Payr at the 44th Congress of the German Surgical Society in April 1920.

The most difficult cases are those on the border-line between obstinate constipation and chronic intestinal obstruction, and the indications for operation, apart from those deduced from the signs of intestinal obstruction, are difficult to define. Payr enumerated a great number of the causes of intestinal obstruction, many of which are only revealed on exploration, but in attempting to classify them the same mechanical cause of intestinal obstruction appears in more than one list. After all, Payr ended by simply enumerating types of operations—the separation of adhesions and the removal of compression; the fixation of mobile organs; the reduction by suture of dilated viscera; anastomoses; intestinal exclusions; intestinal excisions; artificial fistulae, temporary or permanent; plastic operation on the abdominal wall and floor of the pelvis; rectal and anal operations. For obstinate constipation, apart from definite signs of obstruction, the only procedure he emphasized was that of forcible dilatation of the anus.

J. W. Smith described in 1913 operations for atony and prolapse of the large intestine, and after 7 years reported the later results, altogether, of 32 cases, 2 of which were fatal. He had communicated with the 30 survivors and received reports from 26. In 5 cases of dilatation of the caecum, after plication and fixation of the caecum, 4 had proved complete successes. One continued well and had worked at munitions for four years; then there was recurrence of symptoms and he performed hemicolectomy, which after six months continued a success. Hemicolectomy was performed in 12 cases: 1 died on the sixth day from leakage at the sutures, 3 continued in good health, and 8 had improved; 3 of these had to be careful as to diet to avoid gastric disturbance, 1 complicated by chest disease had only slightly improved. The later operations, in which end to end was substituted for lateral anastomosis, showed better results; 7 cases were submitted to total colectomy: 4 had completely recovered, 2 were much better and 1 no better.

A female, aged 28, had suffered for 8 years from constipation complicated by vomiting. For two years she had become so weak as to be unable to stand or walk. The stomach was dilated, being dragged down by a distended and prolapsed colon; the appendix was bound down and had a V-shaped kink. The ileum, six inches from its termination, was united to the pelvic colon by lateral anastomosis and all the intervening bowel excised. The patient replied, 'I am pleased to say the operation you performed has been very successful. I keep well in health, not exactly robust, but have been working as a glove machinist for the last three years.'

A female, aged 42, had suffered for twenty years following the birth of her one child. Severe constipation was accompanied by frequent vomiting, uterine prolapse, and haemorrhoids. During two previous years she underwent four operations, the removal of piles, bilateral oophorectomy, ventrifixation of the uterus, and fixation of the left kidney. Pain and constipation were even worse afterwards. She had been confined to bed, had attempted her life, and was weak, worn, and depressed. Lateral anastomosis between the ileum and the pelvic colon just above the rectum, followed by excision of the colon, was performed, and she left hospital 23 days later. The operation was done in 1912, and seven years later she attended a clinical meeting. She said she was then better than ever before in her life, she could eat anything and had not taken a laxative since the colectomy. She had started work in a cotton mill six months after, and had recently divided her day between cleaning offices and her own housework.

Taylor's account of 8 cases exhibits the influence of Metchnikoff and Lane's prejudice against the colon by adopting for various cases of chronic obstruction one and the same operation, viz. the excision of the large bowel including the caecum and pelvic colon, followed by an end to end union of the ileum to the commencement of the rectum.

*Case I.* Had prolapse of the ascending, transverse, and descending colon. Two years after the operation he reported that he was employed by a shipping company, and said, 'I believe the operation to be a great success. I am in good general health. I get no pain after eating as before the operation.'

*Case II.* Had the termination of the ileum dilated to the size of a normal stomach with the lumen of the caecum and first part of the ascending colon narrowed by being thrown into folds as the result of colitis polyposa. Ten weeks after the operation he was able to play football; six months after his bowels moved three times a day.

*Case III.* Had suffered from constipation, which was not improved by removal of the appendix. Four years later he began to suffer from ulcerative colitis, passing blood and mucus, which increased in the following two years until he had become very thin and weak, with 12 motions a day. Under caecostomy and irrigation he improved, but the caecostomy opening being allowed to close, he relapsed. After the operation he became fit for light work and continued to improve during six months after his discharge from the hospital.

*Case IV.* Had a carcinoma in the centre of the pelvic colon, which caused acute intestinal obstruction, and perforation of the caecum. Temporary relief was given by putting a Paul's tube into the caecum and draining the abdominal cavity. Three weeks later the excision and end to end union was carried out. The general health continued good for 18 months, when metastatic growth in the liver and base of the skull appeared.

*Case V.* Was a similar one up to the recovery from the excision; there was no further report.

*Case VI.* With a faecal fistula following a gunshot wound of the transverse colon, recovered after excision of the whole colon, but there was no report as to his motions subsequently.

*Case VII.* Had been an invalid for years, just able to walk quietly about in her garden, as the result of indigestion. She was seized with acute intestinal obstruction caused by volvulus of a mobile caecum. The caecum, which had become gangrenous, with the ascending colon was excised and an end to end union made between the ileum and transverse colon. The patient recovered, but did not improve in health or increase in weight.

*Case VIII.* After suffering from constipation for many years, had the appendix removed, when it was discovered that the colon was badly prolapsed. Some months later, as no improvement had followed, the caecum and ascending colon were excised, and the ileum joined to the transverse colon. She was comfortable for 18 months, after which constipation recommenced, set up by adhesions producing a kink in the small intestines. The adhesions were freed and ileo-sigmoidostomy performed. This made the patient worse, owing to collection in the loop intervening between the anastomosis. Finally, Lane removed the remainder of the colon and joined the ileum to the upper end of the rectum. From this the patient was at the time of the report recovering well.

Whilst the last case is the one most definitely in favour of complete colectomy, in none of the series is there any account of the number of motions per day consequent upon the direct communication set up between the ileum and rectum.

In the opinion of Lane and his followers no less an operation than complete colectomy is satisfactory. Against this may be set 19 cases reported by Brewster, in which the ileum was anastomosed with the transverse colon, and only the end of the ileum, the caecum, ascending colon, and the beginning of the transverse colon excised. Brewster's cases included a number ef epileptics suffering from obstinate constipation. The operation relieved the constipation and improved the general health without materially influencing the epilepsy.

*Case I.* An epileptic, aged 11, had a largely dilated caecum, chronic appendicitis, and adhesion about the hepatic flexure. He recovered well, was relieved of the constipation ; the epilepsy returned after two months.

*Case II.* A woman, aged 40, had had appendicectomy 12 years before. A dilated mobile caecum was found. One year after the operation she was entirely free from the previous constipation and pain.

*Case III.* An epileptic, aged 22, under X-ray examination presented stasis at the hepatic and splenic flexures. Following the right colectomy there was a marked improvement in the general condition, owing to freedom from constipation, and there was some diminution in the epileptic seizures.

*Case IV.* Had had, two years before, a lateral ileo-sigmoidostomy, which was followed by persistent nausea, frequent vomiting, and the filling of a dilated and mobile caecum with faeces. After the right colectomy, together with excision of the anastomosis and a closure of the opening in the sigmoid, she was entirely relieved, in three months she gained 15 lb. in weight, and seven months after underwent a normal labour.

*Case V.* A woman, aged 52, had had a lateral ileo-sigmoidostomy five years before, after which she suffered from faecal distension of the ileum and caecum, below the anastomosis with the sigmoid. After the same operation as Case IV the patient somewhat improved, but continued to suffer from a degree of constipation.

*Case VI.* Suffered from intestinal stasis, or rather chronic obstruction, caused by a dilated and mobile caecum with adhesions in the region of the hepatic flexure. Entire relief followed the operation.

*Case VII.* An epileptic girl, aged 18, with chronic constipation, was not improved by right colectomy.

*Case VIII.* A boy, aged 3½, had had appendicectomy for intestinal stasis a year before. Three months after the right colectomy the mother reported that the child was normal.

*Case IX.* An epileptic, aged 25, operated upon for constipation, after right colectomy resumed work, and during the subsequent three months there was no return of the epilepsy.

*Case X.* An epileptic, aged 8, had the caecum dilated and mobile, the appendix inflamed, and adhesions extending over the ascending and commencement of the transverse colon. After right colectomy the intestinal stasis disappeared and the general condition improved, but the epilepsy continued.

*Case XI.* A woman aged 30, poorly nourished and extremely constipated, had had for a year occasional attacks of nausea and vomiting. There was a large and mobile caecum, adhesions about the hepatic flexure, and scybala in the colon. Six months after the right colectomy she reported that the constipation had been entirely relieved.

*Case XII.* An epileptic, aged 35, had been always constipated owing to a dilated caecum and ascending colon due to adhesions. Ten months after the right colectomy it was reported that the constipation was entirely cured, the general condition had improved, the epilepsy persisted.

*Case XIII.* A man, aged 23, for 5 years an epileptic, had the epileptic attacks associated with indigestion and constipation. The right colectomy entirely removed the constipation and the general condition markedly improved but the epilepsy continued.

*Case XIV.* An epileptic, aged 21, with a large and mobile caecum, a chronically inflamed appendix, enlarged mesenteric glands, and adhesions about the hepatic flexure, was influenced by the operation in the same way as the preceding case.

*Case XV.* An epileptic girl, aged 12, with constipation and pain in the right lumbar region, had a large mobile caecum, a long mesentery, chronic appendicitis, vascular adhesions, and enlarged mesenteric glands. The constipation was markedly relieved, the epilepsy continued.

*Case XVI.* An epileptic woman with constipation had a large distended caecum, chronic appendicitis, and adhesions about the hepatic flexure. She recovered from the operation but was lost sight of.

*Case XVII.* A woman had severe constipation for 20 years with recurring pain in the upper abdomen and was poorly nourished. The condition found was much the same as in the preceding case. She reported a year after the right colectomy that she felt cured.

*Case XVIII.* An epileptic aged 20, with constipation had a dilated end of the ileum, a mobile caecum and ascending colon. Along with relief to the constipation and general improvement, the epilepsy continued but the attacks were milder.

*Case XIX.* A woman aged 22, who had been an epileptic for a year, had marked constipation with dull pain in the right lumbar region which was worse after the epileptic attacks. There was a mobile caecum, chronic appendicitis, and adhesions over the ascending colon. Right colectomy removed entirely the constipation and the general condition improved but the epilepsy continued.

The most noteworthy feature of Brewster's cases was the absence of any deaths in spite of the many cases of epileptics in bad condition. In nearly all the constipation was quite relieved and the general condition improved. There was no definite improvement as regards the epilepsy even where the attacks seemed to be closely associated with the constipation. But the patients were able to bear the attacks better and in a few the operation coincided with a temporary relief. Thus Brewster's results are opposed to Lane's contention as to the necessity for total colectomy.

Schoemaker, in 68 cases, found the cause to be pericolitis membranacea. The general symptoms had been pain on the right side of the abdomen with tenderness from the region of McBurney's point upward towards the margin of the ribs and across towards the middle line, together with a soft tumour-like resistance, and signs under X-rays of stasis in the ascending colon. The caecum, ascending colon, and to a variable extent the first part of the transverse colon were found covered by a veil of fibrous tissue. Some consider this membrane congenital and the stasis secondary, others hold that the pericolitis is secondary to the constipation, infective organisms or their toxins spreading through the intestinal wall to set up local peritonitis. In the 68 cases he excised the caecum, ascending colon, and part, about 12 cm., of the transverse colon, joining the ileum and transverse colon end to end. Two patients died, one of embolism and the other with signs of prolonged shock, in whom a post-mortem examination was refused. Fifty of the patients were followed up; 32 were quite free from abdominal disturbance, 8 had improved but still had some pain, 10 were not benefited—they still suffered from constipation and pain on the right side.

The examination of the intestine excised showed no sign of colitis; there were no changes in the mucous membrane, muscular or serous coats. The fibrous membrane could be readily raised from the serous coat and consisted of a cellular connective tissue with numerous thin-walled blood-vessels, but with no signs of leucocytes or organisms. The membrane, therefore, appeared to be congenital in origin. In the course of development, the caecum as it descends from the hepatic region tends to become free, whilst the ascending colon with the proximal part of the colon is fused with a layer of parietal peritoneum. In the cases cited the caecum was not dilated or specially mobile, so as to drag on the ascending colon. Indeed, in some, the caecum was quite high up, covered, along with the commencement of the transverse colon, by a markedly vascular membrane.

Short of excision a mobile caecum and ascending colon may be plicated in a simple fashion after appendicectomy by suturing together the anterior and external taeniae as far up the ascending colon as seems desirable. Ten Horn, of Ghent, has reported recently as to the favourable results. It is merely a prolongation of the suture burying in the stump of the appendix. Waugh, in 180 cases, adopted a more extensive operation, requiring a much freer abdominal incision, and with the result of rendering the caecum and ascending colon more fixed than is natural. Waugh incised the parietal peritoneum to the outer side of the caecum and ascending colon from the brim of the pelvis to the level of the duodenum. After raising the outer edge of this peritoneal incision as a flap, he cleared out fat from the front of the lumbar muscles, laid the caecum and ascending colon in the hollow so made, and sutured the peritoneal flap over the outer side to the anterior taenia.

The increase of coarse vegetable food in the diet has apparently caused a notable increase of cases of volvulus of the sigmoid flexure. This has been noted by Neugebauer in Russia, by Neudörfer in Germany, by Guimbellot and Okinczye in France. If the case is seen whilst there is only pain and constipation, and the sigmoid flexure is merely mobile, excision and end to end union should be carried out without delay. If, unfortunately, volvulus has occurred and set up acute intestinal obstruction, then incision, with end to end union, together with a temporary caecostomy, is best; failing that, the excision of the volvulus, after tying in a Paul's tube above and below, followed later by closure, which, however, is difficult to accomplish. The proposal attributed by Neudörfer to Pachhammer in 1912, viz. to make an anastomosis between the proximal and distal arm of the volvulus, is likely to fail. After temporary relief a further twist of the volvulus may involve the anastomosis and set up recurrence of the obstruction. An incision of the volvulus is open to the danger that the orifice may be situated below the upper end of the obstruction.

One of Okinczye's cases is instructive. In 1915 a man of 47 had an attack of intestinal obstruction which passed off spontaneously. In June 1916 a more prolonged attack was treated on the 12th day by caecostomy, but as this did not relieve him, ten days later the sigmoid flexure was opened. From this faeces escaped regularly, but from the lower end, and a prolapse of 20 cm. of the sigmoid supervened. An X-ray examination then showed a volvulus of the sigmoid with the caecum and ascending colon much dilated. At last, in November 1920, the volvulus was excised and an end to end suture closed the opening, which was followed by an uncomplicated recovery. Against the foregoing may be set the case recorded by Guimbellot. A woman aged 26 had been constipated since childhood, four to five days intervening between her stools, attended with pain, especially in the left hypochondrium. Acute intestinal obstruction supervened, and 36 hours after the onset a volvulus of the sigmoid was exposed, the loop being distended to the size of a man's thigh. The volvulus was excised and the two ends united. There was a spontaneous motion on the sixth day. She was discharged after a month. Four months later she was well, but with some constipation and colicky pains, an X-ray examination discovering a delayed passage through the colon.

**Conclusions.** When a case of chronic intestinal stasis presents difficulties in diagnosis, the recommendation of Greig Smith may be adapted. He advised that a surgeon, when in doubt as to whether a patient was suffering from acute intestinal obstruction calling for operation, should sit down by the bedside and observe the patient for an hour or more.

After a purge has been administered the progress of its effect along the intestinal canal may be followed. Variations in the movements and distension of the bowels, changes as regards cutaneous hyperaesthesia, muscular rigidity, reflexes, and deep tenderness may be noted and then compared with the patient's sensations. Similar observations may be made after the patient has swallowed some gruel containing bismuth or barium sulphate, the course of the intestinal contents may be observed through the X-ray screen, and photographs may be taken at other junctures than those fixed beforehand.

Hitherto the examination of the wall of the colon removed for chronic constipation has often been barren of results. In a case of a caecum and ascending colon removed by Spencer, Keith found in the submucous tissue a remarkable collection of large branched cells loaded with pigment, melanin chromatophores. It is possible that in the future further evidence may be forthcoming as to pathological fine alterations in the neuro-muscular mechanism of the large intestine. Whether partial or total colectomy be done, it is not clear why it has been usual to sacrifice the ileo-caecal valve. The preservation of the valve might well have two advantages, the prevention of the ascent of bacteria so as to disturb the juice digestion in the ileum, and the prevention of too frequent motions.

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## MELANIN, MELANOMA, MELANOTIC CANCER

Recent observations have increased knowledge regarding the pigment melanin, a substance which has presented special difficulties under chemical examination. These observations have an important bearing upon questions relating to pigmented benign formations, melanomas, as well as to the malignant melanoblastomas or melanotic cancer.

The following may be noted as some of the steps by which advances have been made.

In 1887 Thormählen originated the idea of a colourless melanogen by finding that the urine of a woman suffering from secondary melanotic cancer, when treated with sodium nitroprusside and caustic potash, turned blue-green. There were, however, substances in the normal urine of cattle and horses which gave the same reaction. Herzog and Zeller examining urine from a similar case at a more advanced stage, when the urine had become brown from melanin, distinguished the reaction of melanin; the solution turned green with the Thormählen test, and black with perchloride of iron, whereas previously colourless melanogen turned with the Thormählen test a steel blue or Berlin blue.

In 1896 Bertrand, examining the juice of plants which are the source of black Japanese lacquer, found that a kind of melanin was produced by oxidation through the aid of an enzyme. This enzyme being isolated acted on tyrosin, turning it first a violet-red, then causing a black deposit of melanin. The enzyme, being considered an accelerator of the oxidation of tyrosin, was named tyrosinase.

Attention was also directed to the blood of those insects which turns black on exposure to light. Hollande demonstrated the presence of a tyrosinase in the blood of such insects; it was also found in the ink-sac of *Sepia*. In contact with air this tyrosinase accelerated the oxidation of a chromagenic material, melanogen, to form melanin.

In 1909 Meirowsky found that pieces of skin taken *post mortem* from brunettes, also frozen sections of the same, were darkened by exposure to a quartz lamp or by heating up to 56° C. Microscopical examination of a section showed that the darkening was produced by a heaping up of pigment in the basal cells of the epidermis. Portions of skin taken *post mortem* from a case of Addison's disease and kept in an incubator for 5 days underwent a still greater degree of darkening. In 1910 Königstein, in order to dispose of the objection that the above was a post-mortem effect, excised both adrenals from dogs. In animals which survived a pigmentation of skin occurred, similar to that taking place in Addison's disease. The darkened patches of skin, removed *intra vitam*, and placed in an incubator for 48 hours at 50° C. were made much darker, and if the sections were boiled in water for 5–7 minutes before being placed in the chamber, they became darker still.

In 1914 Bittorf demonstrated that the frozen sections of skin from Addison's disease were similarly darkened by dilute solutions of tyrosin and of adrenalin, the latter being the more active. In a solution of adrenalin, 1 in 1,000, the sections were rendered quite black in 4–5 hours; in a solution, 1 in 100,000, in 21 hours the sections had become distinctly darkened. In the case of a soldier who had been shot through the loin, and in whom it was conjectured that the adrenals might have been injured, Leschcziner found that exposure to a quartz lamp caused the skin so exposed to darken in a way which persisted after 7 months. Pieces of this skin, cut out *intra vitam* from the man, darkened in the tyrosin and adrenalin solutions, like the skin from Addison's disease.

Bloch discovered that 3, 4-dioxyphenylalanin—for short 'dopa'—in an aqueous solution, 1 in 1,000, could be used as a test for the presence of tyrosinase in the protoplasm of the cells of the malpighian layer of the epidermis, by which pigment granules of melanin were formed.

**Melanin.** Melanin is a pigment which, almost absent from the skin of a blonde not exposed to the light, is the marked characteristic of the stratum germinativum of the epidermis of the negro. The total quantity of melanin under normal conditions in the skin of a negro has been estimated at not more than 1 grm. In a fresh melanotic cancer the melanin may amount to 7–10 per cent. by weight of the whole; the total quantity of melanin produced in cases of generalized melanotic cancer may reach from 300–500 grm. The ink of a squid consists of melanin; as the animal continues to discharge it under repeated irritation the colour is weakened until finally a colourless fluid is discharged from the sac.

Chemical examination has proved that melanin is an iron-free pigment, unconnected in origin with haemoglobin. As distinguished also from haemoglobin, it contains sulphur; in the material from a melanotic cancer as much as 10 per cent. of sulphur has been found, in the melanin from a squid as much as 12 per cent.

The source of melanin is the proteid molecule, and the amino-acids concerned in its formation are probably the sulphur-containing cystin, the phenolic tyrosin, and the indol-derivative tryptophane. Dioxyphenylalanin, the so-called 'dopa', is closely allied to tyrosin, but contains an additional phenolic hydroxyl, being a catechol derivative. It is an amino-acid which has been obtained from plants readily forming black pigment when injured—e. g. the broad bean. It is very readily blackened by oxidation in the presence of tyrosinases, and can therefore be used as a test for such enzymes.

According to Bloch, the normal as well as the pathological pigmentation of the skin is produced by the epithelium of the stratum germinativum, in deep pigmentation also by the superjacent cells of the stratum spinosum, also by the deep layer of the cells of the hair follicle and of the hair papilla, the latter determining the colour of the hair. These are the normally active pigment-forming cells. Under normal conditions the cells are quiescent and the pigment formation small. The same applies to the cells of a stationary melanoma. Under abnormal conditions the cells become active and there is more active pigment formation. The active pigment formation then occurs in cells which are undergoing division. Indeed in a rapidly growing melanotic tumour the division of cells is in advance of the formation of the pigment, so that some of the secondary growths are not pigmented.

The formation of the melanin pigment occurs in the protoplasm of the cell, the nucleus does not take an obvious share in the process. The dioxyphenylalanin or 'dopa' solution serves as a test for the presence of tyrosinase. Bloch explains that there exists in the cells of normally pigmented skin an enzyme which blackens with 'dopa', and that this enzyme is absent from the skin of albinos and in the non-pigmented patches of the skin of an animal elsewhere spotted by pigment. Upon the relative amount of this oxidizing enzyme depends the reaction to a stimulus such as light. Hence may be explained the variations in the degree of pigmentation produced by the action of rays of light on the skin of different individuals. Also it may be supposed that in Addison's disease there is a failure on the part of the suprarenals to form adrenalin from the mother substance. As a consequence there is an accumulation of the latter, which, collecting in the epidermal cells, is there converted by the tyrosinase into melanin.

**Melanin pigment cells.** The study of the distribution of the melanin pigmented cells of vertebrates and invertebrates shows that it occurs most commonly in cells derived from embryonic epiderm, and particularly so in man. This includes the skin and appendages, both above and underneath the shell of a crustacean, and the choroid coat in the eye. Besides there are found pigmented cells around the abdominal cavity or coelom, and along the course of blood-vessels and nerves. In all of these places the areas of pigmentation are not strictly defined, but there are found outlying cells in addition. Besides the skin and choroid coat of the eye, there are melanin pigment cells in the olfactory epithelium and in that lining the labyrinth. Cells may be found which have apparently wandered out into the sclerotic. The occurrence of a melanotic tumour growing from the pia mater or choroid plexuses of the brain may be explained as originating in cells which have been derived from embryonic epiderm, or represent pigment cells in the sheaths of nerves and arteries in lower animals. A melanotic tumour of the palate may be connected with the pigmented patch in the mouth and throat of, e. g. some dogs.

The pigmentation of cells around the primitive coelom may afford an explanation of the pigment cells of the suprarenals, melanotic patches may be seen on the surface of the gland ; in some birds and animals pigment cells have been noted in the tunica albuginea of the testes. In domestic animals melanotic growths arise in the retroperitoneal tissue ; a melanotic growth of the ovary is more often secondary, yet the above gives a possible explanation of a primary melanoma of the ovary. In one case it originated in an ovarian dermoid cyst. In the thorax, of sheep in particular, the endocardium and the endothelium of the large vessels are spotted with pigment, from which it is likely that a primary melanotic tumour may arise.

In the embryo the source of the melanin pigment is not in the ovum. The frog's ovum is pigmented but not so the ova of tritons and salamanders, in which the melanin pigment appears after the formation of blood. The development of the melanin pigment cells can be watched in the transparent leptocephalidae ; also the choroidal pigment in the development of the eye of vertebrates ; it originates from non-pigmented cells.

**The chromatophores.** Melanin pigment is contained in large cells with multiple branches lying amongst epithelial cells, also beneath the epithelium in the cutis and elsewhere. Chromatophores are seen in invertebrates along the blood-vessels, having amoeboid properties, in *Amphioxus* along the course of the nervous system, in crustaceans around the intestines. In melanotic cancer the pigmented cells may be spindle-shaped or rounded. Such chromatophore cells contain much more pigment than any individual epithelial cell.

A precisely opposite explanation to the view that the epithelial cell of the stratum germinativum forms the pigment is that the pigment is formed in these chromatophore cells, which are mesoblastic in origin.

Those that believe that these cells are merely chromatophores, pigment carriers, which take up the pigment from the epithelial cells or melanoblasts, to carry it away along the lymphatics to the lymphatic glands, note that chromatophores are absent under patches of vitiligo and nonpigmented scars. But at any rate, when melanotic cancer is developing and the cells are rapidly dividing. these mobile chromatophores become capable of forming pigment in distant metastatic growths.

That cells of mesoblastic origin in insects can form melanin in their protoplasm was stated by Hollande in the case of insects, the blood of which blackens on exposure to the air. The vacuoles of the phagocytes, into which particles like bacteria or inorganic granules are taken, contain plasma and the tyrosinase. Under the influence of light, owing to the presence of a chromagenic melanogen and a tyrosinase enzyme, granules of melanin are formed in the vacuoles. Subsequently the melanin leaves the phagocyte, passes away in the blood, and is taken up by other cells.

**The structure of melanomas and melanotic cancers.** Passing on to abnormal collections of the melanin pigmented cells, melanotic moles and patches have two arrangements of cells which, however, may be combined. In one, characteristic of the pigmented moles of the skin, the pigmented cells are arranged in rows more or less vertical to the surface, somewhat resembling the cortex of the suprarenals; or the cells have a somewhat alveolar arrangement. Outside these cells are scattered chromatophores. It is especially in melanotic cancers derived from the skin that the alveolar arrangement persists and is continued in the metastatic growths, particularly of the lymphatic glands. This suggests an epithelial origin, and that the malignant growth is a carcinoma. With this accords the tendency to spread first to the lymphatic glands corresponding to the area.

The other type of melanoma suggests that the chromatophores are the basis. If the melanomatous spot is in loose tissue, the cells are large with multiple branching processes. In new growths, especially those arising in the internal organs of animals, the cells resemble those of spindle-celled and round-celled sarcomas, as if the above mentioned cells had, in the course of multiplying, become compressed.

Referring to veterinary pathology, there is clear evidence that in cats and dogs melanotic cancer commences primarily and almost exclusively in the skin and eye. In horses, especially grey horses which become white, the common primary growth is from the skin of the region of the anus. In the majority of reports concerning horses, cattle, and sheep, no attempt is made to note the situation of the primary growth. A source in a suprarenal capsule is particularly ignored. Hence there are returns of melanotic cancer of horses in the muscles, lymphatic glands, heart, lung, spleen, parotid, in cattle in the stomach, in sheep in the bones. Statistics given by Lubarsch illustrate the frequency of melanotic cancer in the Berlin Veterinary Institutions, 175,745 horses, cancer and sarcoma in 527, melanotic cancer and sarcoma in 226, i. e. 42·88 per cent. In grey and white horses there is definitely an increasing tendency with age, which is not the case in human beings. An old explanation of the predisposition in white horses is that the chromatophores overloaded by the withdrawal of pigment from the hair and skin fail to be excreted by way of the blood.

**Diffused melanotic pigment.** Matsunga's observation is important in relation to the cases of melanotic cancer in which a diffuse pigmentation occurs. He made a post-mortem examination on a man, aged 41, in whom a pigmented mole on the forehead had been noted, for four years before its removal, to be exhibiting signs of growth. It had been removed one year before death, along with large glands from the neck. At the time of removal the primary growth had already ulcerated, and beyond the outline of the tumour, when excised, there appeared a diffuse brownish pigmentation of the connective tissue. At the examination after death there were found numerous metastases and in addition a generalized pigmentation of the skin of a diffused brown colour. Much of the pigment was found in spindle-shaped and stellate cells, and the 'dopa'-reaction of Bloch was yielded both by epithelial and connective tissue cells. By this it was shown that fixed connective tissue cells, as distinct from wandering cells, were pigmented and yielded a positive reaction. Besides the fixed connective tissue cells, endothelial cells of blood-vessels, reticulum cells in lymphatic glands, also epithelial cells of the kidneys, lungs, and thyroid gland, all gave a positive 'dopa' reaction.

These observations indicate that a melanin-producing enzyme can be discharged in solution from the tumour cells, which is carried off by the blood, and, arriving at non-pigmented mesoblastic cells, is capable of producing the pigment. This brings the diffuse pigmentation in the case of melanotic cancer into line with that of the pigmentation following Addison's disease. It further points to the starting of the primary malignant development in a previously quiescent mole as being connected with a production to excess of the pigment-forming enzyme. In relation to the origin of cancer in general, the cause of melanotic cancer is intimately bound up with the melanin pigment.

**The pigmented mole on the skin.** There is at any rate one established fact—that to prevent melanotic cancer from arising in man, any pigmented mole or patch which shows the slightest tendency to change should be cut out. Moreover, a surgeon, when called upon to make an incision under an anaesthetic, should take the opportunity of removing a mole existing on the neighbouring skin.

The danger following upon the irritation of a pigmented spot on the finger or beside the nail, the melanotic whitlow of Hutchinson, is well known. Yet owing to the ubiquity of these moles the possibility of complication may be overlooked.

A small boy, a brunette, both the mother and father being South European brunettes, had, as well as his parents, many moles, including three on the toes of one foot. One of the black spots on a toe had become inflamed and commenced to ulcerate. It had been seen by several medical practitioners, who had all diagnosed the condition to be the result of frostbite, in spite of the ulcer being at the base of the toe, the circulation of the feet good, and the child well cared for. When cut out the ulcer was found to be a commencing melanotic cancer, the other two patches quiescent melanomas; the glands in the groin showed small-celled proliferation with some large cells containing melanin pigment.

Even more dangerous are the moles about the genitals and anus.

Holland, in 1908, collected 52 recorded cases of melanotic cancer of the vulva and the vaginal orifice. The cases had nearly all been treated too late, only one being known to be free from recurrence three years subsequent to the removal. The records were defective on important points, viz. the origin in a pigmented mole and the early infection of the lymphatic glands. A further difficulty was that some were probably metastatic in origin. Doran, in 1905, was the first to distinguish a melanotic growth on the vulva, secondary to a melanotic cancer of an adrenal, and he subsequently mentioned three other similar cases.

Miescher examined enlarged crural lymphatic glands which had become affected from a pigmented mole on the thigh after it had turned malignant. The glands exhibited the alveolar type of melanotic cancer and some of the tumour cells gave the 'dopa' reaction, others did not. The cells which gave the positive reaction were cells which could be seen to already contain some pigment and were of epidermal origin.

**Melanoma and melanotic cancer of the eye.** Apart from the regular pigmentation, melanomatous spots are seen in the choroid and in its neighbourhood. Such patches are very common on the iris of horses. They also occur in non-pigmented tissue such as the conjunctiva.

The choroid pigment in the embryo appears to develop in previously colourless cells derived from the epiderm, and melanotic cancer, when it arises, starts in these pigmented cells. But histologically both the primary growth and the metastases have the general structure of spindle- and round-celled sarcoma rather than of alveolar cancer. As differing from the pigmented basal cells of the epidermis, the cells of the choroid fail to yield the 'dopa' reaction. Bloch's explanation of this is that the choroid cells are entirely quiescent, no pigment metabolism going on in them under ordinary circumstances.

Moore has carefully described the quiescent melanomatous patches of the choroid as seen by means of the ophthalmoscope, and in one case he had the opportunity of examining the eye, after death from a totally unconnected cause. The melanomas were in four cases discovered during routine examination, and consisted of deeply pigmented patches of the choroid in the neighbourhood of the optic disk, with normal retinal vessels in front. In the eye examined after death there was found no essential difference in histological structure from melanomas elsewhere. In the same eye, in the ciliary muscle, was a group of melanin chromatophores such as is met with in the eyes of negroes.

The foregoing cases had presented no disturbance of vision, but Moore quoted previous descriptions of appearances of such patches suggestive of a commencement of malignant changes. A remarkable feature of melanotic cancer of the eyeball is the delay in the appearance of metastases, and that not in corresponding lymphatic glands, but especially in the liver, followed by melanuria. A delay of ten years or so has been many times reported, and Moore quoted a case which survived to die of abdominal metastasis 17 years after the removal of an eyeball for melanotic cancer. Were it not for the similarity in the appearance and course, a separate new melanotic growth in the abdomen might seem a more likely supposition, rather than a metastasis so long after the primary disease.

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W. G. S.

## ACUTE SUPPURATION ABOUT THE WRIST TREATED BY INCISION DIVIDING THE ANNULAR LIGAMENT

Septic infection of the hand being neglected for a week or so, acute suppuration becomes established in the palm and spreads among the tendons into the lower third of the forearm, also to the wrist and carpal joints. The question then is whether the patient's life can be saved, short of an amputation, by incisions which will arrest the septic inflammation. The resort to several short incisions and the insertion of drainage tubes, granted that the process of suppuration becomes arrested, generally renders the hand useless for all finer movements. A more extensive operation, imitating the operation for tuberculous disease introduced by Lister, has in the two cases quoted below, recorded by Helferich and Muraud, enabled much finer movement to be gained. Patients suffering from tuberculous disease involving the wrist, carpus, and the lower third of the forearm, after the Lister operation have been enabled, e. g., to write a remarkably fine hand. When treating acute suppuration by making small incisions and inserting drains, it has been customary to pass tubes from the flexor aspect of the forearm, under the annular ligament, and out by the palm. The flexor tendons become firmly glued together and all movement of the tendons is completely and permanently lost.

Chaput reported that in five cases he had removed the carpal semilunar and passed a tube through from the flexor to the extensor aspect. One man was aged 68, two men aged 65, one woman aged 60, and another 55. Amputation was thus avoided; the hand healed, but all the fingers were firmly ankylosed 'en griffe'.

V. Saar and Schamberger recall the old names for the lines in the skin of the palm, the longitudinal midline continued over the wrist-joint, the so-called *linea fortunae*, the line deviating from it below the wrist to skirt the thenas eminence, the *linea vitalis*, also the two transverse lines, the distal one, the *linea musalis*, and the proximal, the *linea cephalica.* These lines form landmarks for the structures in the palm. A longitudinal incision a few millimetres to the ulnar side of the *linea fortunae* has the ulnar nerve and artery to one side and the median nerve to the radial side. If the incision begins above the *linea cephalica* the arteries of the palmar arch may be avoided, and no tendon is injured when the incision is continued up through the annular ligament.

**Helferich's case.** A man aged 32 injured the little finger of his right hand. Acute swelling of the hand and lower two-thirds of the forearm followed, and the axillary glands became enlarged to the size of hazel-nuts. Seven days later, under general anaesthesia, and after applying a tourniquet, an incision was made to the ulnar side of the middle line longitudinally through the annular ligament, without injuring the ulnar nerve or artery or the deep palmar arch. Pus was found among both the superficial and deep flexors, also along the interosseous ligament to above the middle of the forearm. The whole was cleaned with the aid of a 0·6 per cent. salt solution; after loosening the tourniquet, bleeding-points were tied, and then the wound was filled with iodoform gauze. The gauze remained *in situ* for ten days. The temperature at the operation was 39·1° C., on the day after 37·3–39·5° C., and on the second day 37·6–38·8° C., it became normal on the third day and remained so. Twelve days after the operation, again under a general anaesthetic, and, after applying a tourniquet, granulations were scraped away, the margins of the skin undermined, the long incision sutured. There remained the primary lesion of the little finger where the flexor tendon had sloughed. The patient was discharged healed after two months. 3½ months after healing the man was examined: he had been some time at work, he could flex all his fingers well except the little finger. The united incision was firm, there was no weakness of the annular ligament, the state of the muscles of the forearm was equal to that of those on the left side.

**Muraud's case.** Muraud reported that a nurse, aged 52, punctured her left thumb whilst dressing the stump after an amputation through the thigh for multiple wounds infected by streptococci. A small whitlow formed, which was aggravated two days later by the left hand and forearm being accidentally squeezed. Eight days after the puncture acute suppuration had extended to the palm and above the wrist, also to the dorsal aspect. Above streaks of inflamed lymphatics stretched upward to inflamed axillary glands. A long median incision was made, extending from the palm through the annular ligament to the junction of the lower and middle third of the forearm. A large quantity of pus escaped from over and among the tendons. Another longitudinal incision on the dorsum exposed the extensor tendons, also bathed in pus. From both sides holes led into the wrist-joint and among the carpal bones. All the carpus was removed except the trapezium and pisiform bones. The pus yielded a pure growth of streptococci. The after-treatment by the Carrel Dakin method of irrigation was continued for a fortnight, after which the hand was fixed in plaster, with the wrist dorsiflexed and movement of the fingers begun. Four months after the operation the patient could use her thumb and fingers sufficiently to grasp a book, could dress herself, do her own hair, insert hairpins and hold a glass to drink with the affected hand. Six months afterwards the thumb could approach to within 1 cm. of the little finger and she could lift a chair with that hand. Fourteen months after the operation she could sew, iron, and embroider, and do many other things; the thing she could not do was to button the opposite glove, owing to general reduction of the movement of the thumb and fingers.

Lecéne, in the discussion on Muraud's paper, commended the procedure which he had adopted since 1912; for such cases drainage above and below the annular ligament led to deplorable results.

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# ABSTRACTS

## SURGERY

**Cernezzi, A.** Contributo alla cura radicale delle grandi ernie ombelicali e degli sventramenti mediani. [**Treatment of large umbilical and ventral hernias.**] *Arch. ital. di chir.*, 1920, **2**, 352.

Plastic operations for the closure of large apertures in the abdominal wall by means of flaps cut from the sheaths of the recti muscles were introduced by Nable (1897), Karewsky (1904), and Polya (1905). The feature common to the three methods was the formation of a more or less extensive flap from the anterior layer of the sheath of each muscle with its base towards the middle line. Nable sutured the two recti muscles in their whole thickness, disregarding the closure of their sheath; Polya, who applied his method to comparatively small hernias only, united the two flaps by means of a purse-string suture and then drew together the external margins of the incisions in the sheaths. Karewsky extended the method to hernias of large size, reflecting the flaps over the aperture, suturing their margins, and completing the closure by suturing in strata.

The relative ease with which the aponeurosis of the external oblique muscles can be approximated, and even superimposed, has led to the introduction of further modifications in these methods. In so far as these involve the isolation of extensive aponeurotic flaps they are regarded by Cernezzi as of doubtful value, since they tend to weaken the abdominal wall not only by reducing the vascular supply of the aponeurosis, but also by altering the functional relations of the abdominal muscles. The operation recommended by Cernezzi himself is very similar to that of Karewsky, although worked out independently. Cernezzi noticed that in cases where suture by strata was impossible with any prospect of satisfactory results, the difficulty experienced in closing the hernial aperture lay in the posterior layer of the rectus sheath: this powerfully resisted traction towards the middle line, while the anterior layers could be readily approximated. The difference in the behaviour of the two layers is explained by the difference in their origin; the deeper layer is, in fact, merely the aponeurosis of the transversalis muscle reinforced by the deep layer of that of the internal oblique, and its fibres run in the direction of the traction applied; the superficial layer is formed from the aponeurosis of the external oblique, and its fibres, owing to their oblique course, allow of a certain degree of lateral deviation. An elliptical cutaneous incision is made over the hernial protrusion and the sac dealt with in the usual way. The sheaths of the recti muscles are next exposed for a long distance above and below the hernial aperture, and cut longitudinally at about a finger's breadth from their internal edge, the incisions being curved obliquely inwards at the extremities. The flaps are reflected towards the middle line and sutured together at their margins. In this way the hernial aperture is closed and the united edges of the flaps serve as a good line of support for the subsequent superficial sutures. The remaining external portions of the sheaths are then brought together and sutured in the middle line, no difficulty occurring in their approximation for the reasons before mentioned. The superficial fibres of the muscles are to be included in the sutures, so that the muscles may be drawn together at the same time. The point of importance in this technique is that the plastic operation should extend far beyond the longitudinal diameter of the hernial aperture, and be proportional to the greater or less degree of diastasis of the recti muscles.

Since 1907 Cernezzi has operated on 16 cases, 8 umbilical and 8 median ventral hernias. Of the 8 umbilical hernias 3 were recurrences in very fat subjects and the results were good in all, no relapses having occurred after periods varying from 5–11 years, and one of the patients having been delivered at term without inconvenience. Of the ventral hernias 3 were spontaneous and 5 followed laparotomy, 2 of them being recurrences which had been treated by other surgeons. The results were good in all cases after 7–12 years. T. W. P. L.

**Pirondini, E.** Pielite larvata, cistalgica. [**Pyelitis larvata cystalgica.**] *Arch. ital. di chir*, 1920, **2**, 502.

Patients with this affection suffer from pollakuria, associated with extremely painful micturition. The increased frequency of micturition is both diurnal and nocturnal, and often presents great regularity; the stimulus occurring, for instance, every hour day and night. The disease is very chronic, and neurasthenia results through prolonged suffering, disturbance of rest, and hopelessness of recovery. The urine is somewhat turbid, and from time to time there may be slight haematuria: pain in the region of the kidney is absent. The clinical picture suggests an obstinate cystitis, either tuberculous or insufficiently treated. Evidences of tubercle are absent, and there is no wasting. Objectively, the most prominent symptom is the extreme pain and desire to micturate produced by pressure on the bladder, whether applied above the pubis or per vaginam. Palpation of the renal regions may reveal a slight tenderness, but this is often entirely absent.

The urine is always turbid, acid, and contains a small amount of albumin and numerous pus cells. The daily quantity may be normal; there is often, however, a slight degree of polyuria. The amount of nocturnal urine is little less than or equal to the diurnal urine, and the normal fluctuation that occurs during the day is less pronounced, the secretion taking place more regularly, with, however, occasional sudden increases as if from transitory retention. When these changes in the secretory process are well marked, as shown in the accompanying figures, and the other symptoms mentioned are present, the diagnosis of cystalgic pyelitis is almost certainly established.

*Urine Collected at Intervals of Two Hours.*

| Normal. | Pyelitis. | Normal. | Pyelitis. |
|---|---|---|---|
| c.c. | c.c. | Sp. gr. | Sp. gr. |
| 31 | 138 | 1022 | 1013 |
| 43 | 120 | 25 | 13 |
| 628 | 365 | 02 | 06 |
| 345 | 200 | 03 | 09 |
| 65 | 196 | 17 | 11 |
| 80 | 180 | 20 | 12 |
| 55 | 170 | 26 | 12 |
| 156 | 1275 | 27 | 11 |

Cystoscopy and catheterization of the ureters are difficult in these cases, owing to diminution in the capacity of the bladder. In the cases in which Pirondini succeeded in using these measures the bladder appeared normal except for slight congestion of the ureteral orifices, and the ureters showed the signs of pyelitis.

It appears probable that the disease may originate in two ways, either as a primary haematogenous pyelitis or as an infection ascending from the bladder, which has become subsequently cured so far as the vesical infection is concerned. In either case the cystalgia is to be explained as a reflex symptom originating in the renal pelvis or ureter.

With regard to differential diagnosis it has to be remembered that in cases of prolonged cystitis with slight or doubtful pyelitis an obstinate cystalgia is more likely to be dependent on a slight residual cystitis of the neck of the bladder than on pyelitis larvata; and that pollakuria with cystalgia is in some instances purely functional in origin.

Satisfactory treatment is difficult, especially in long-standing cases. Distension of the bladder should be carefully avoided, and in washing out the bladder, which, however, is rarely indicated, the limit of tolerance should not be reached and the double current should be employed with the channel of afflux smaller than that of efflux. The treatment generally is similar to that adopted in vesical tubercle; sedatives are preferable to pure antiseptics, and may be administered by the mouth and per rectum as well as directly to the bladder itself. Attempts should be made to lessen the pyelitis, and for this purpose the author has found instillations of collargol useful. Intense painful and febrile reaction follows the instillation, but distinct amelioration results, without, however, definite cure. T. W. P. L.

**Borelli, E.** Ernie inguino-superficiali e diverticoli del sacco. [**Superficial inguinal hernia.**] *Policlin.*, 1920, **27** (Sez. chir.), 341.

Superficial or subcutaneous inguinal hernia, two cases of which are described by the author, is rare. The essential characteristic of the condition is the situation of the sac immediately beneath the superficial fascia, and one of its more constant features is its association with incomplete descent of the testis. The sac itself is frequently bilobed, one portion following the usual course of the hernial protrusion beside the spermatic cord, the other becoming superficial in front of the aponeurosis of the external oblique muscle and being directed externally towards the iliac spine, or upward in front of the sheath of the rectus, or downward into Scarpa's triangle, or inward and backward into the perineum. The former part of the sac is always narrow, empty, partly obliterated, or subdivided by adhesions, and extends for a variable distance into the scrotum, at times, especially when the testicle is not retained, reaching the bottom of the scrotum. The subcutaneous part of the sac contains the displaced viscera when hernia is present, and when empty is usually completely pervious and in free communication with the central portion of the sac. Although usually bilobed, the sac is sometimes single, a condition chiefly met with in cases of acquired hernia. In such cases the sac, being of secondary formation and meeting with some obstacle to its descent along the cord, is deviated *in toto*: in congenital herniae, if the processus vaginalis should offer any obstruction to the descent of the viscera, a lateral diverticulum is formed. In the former case a simple sac, in the latter a bilobed sac results. When superficial inguinal hernia is associated with retention of the testicle, this organ is usually found in the subcutaneous portion of the sac, either free or fixed by remains of the gubernaculum : at other times it is retained in the inguinal canal or immediately outside the external ring, and in this case, when the sac is bilobed, as in the author's two cases, the testis is found near the bifurcation of the sac and in a position to obstruct the passage of the herniated viscus into the scrotal portion.

Various theories have been adduced to explain the occurrence of the lesion ; it is probable, however, that several factors are concerned, and vary in different cases. With a simple sac bent on itself at the external ring, and with the testis in its normal position, it will probably be found either that the external ring is abnormally large, its columns lax, and the inguinal canal directed more forward than normal, or that a badly-fitting truss has allowed the viscera to pass the external ring while preventing their descent into the scrotum. When the sac is bilobed, the testis, usually situated at the point of bifurcation, offers an impediment, and the descending viscus is deflected accordingly ; or, when the testicle is in its normal situation, obliteration or stenosis of the terminal portion of the sac will be found, or some mechanical external cause, such as excessive pressure of a truss. When the testicle is present in the superficial portion of the sac the hernia is probably due to the testicle itself, which paves the way for the subsequent descent of the bowel, and this is the more probable when the abnormal position of the testis is due to an anomalous fixation of the gubernaculum, a condition met with in some cases and indicated by a band of fibrous tissue, containing smooth muscle and elastic fibres, retaining the testis in its new position. Such cases are due primarily to a congenital deviation of the processus vaginalis. T. W. P. L.

## NEUROLOGY

**Trotter, W. On certain clinically obscure malignant tumours of the nasopharyngeal wall.** *Brit. Med. J.*, 1911, ii, 1057.

**Jacod, M.** Sur la propagation intracranienne des sarcomes de la trompe d'Eustache : syndrome du carrefour pétro-sphénoïdal : paralysie des 2^e^, 3^e^, 4^e^, 5^e^ et 6^e^ paires craniennes. [**The intracranial extension of sarcomata of the eustachian tube : syndrome of the petro-sphenoidal junction.**] *Rev. neurol.*, 1921, **38,** 33.

In 1911 Trotter first drew attention to a syndrome of peculiar interest to neurologists, arising from the spread of and the infiltration of surrounding tissues by endotheliomata arising in the lateral wall of the nasopharynx. When these growths project into the nasopharyngeal cavity they are readily observed and give rise to no neurological symptoms, but when there is little or no external projection, diagnosis depends entirely on the recognition of the symptoms of infiltration of the nasopharyngeal wall. These are, in Trotter's experience, remarkably constant. The region of the pharyngeal wall particularly affected is the orifice of the eustachian tube and the prominent cushion below it formed by the levator palati. External to the cartilaginous tube and this muscle lies the inferior division of the fifth nerve, and lateral to this the internal pterygoid muscle. The tumour, which is commonly an endothelioma, appears to originate in the substance of the pharyngeal wall and early involves the eustachian tube, causing deafness; the levator palati, causing defective mobility of the soft palate on the affected side; and then the inferior maxillary nerve, causing neuralgia in the ear, the side of the head, the jaw, and the tongue. Ultimately involvement of the internal pterygoid muscle prevents proper closure of the jaw.

**Deafness** is usually the initial symptom, it is of eustachian tube type and may be relieved temporarily by inflation of the tube; it may not be noted unless examined for.

**The neuralgic pain** is always strictly of fifth-nerve distribution. In one of Trotter's cases upward extension of the growth into the sphenomaxillary fossa had involved the second division of the fifth nerve. Objective sensory change appears some weeks or months later than the pain, which is very severe and may, in the absence of other detected signs, give rise to a diagnosis of trigeminal neuralgia.

**The palatal defect** is due to direct involvement of the muscle, and is most apparent when the palate is at rest, for while the muscle may still be able to contract, its relaxation is imperfect or delayed. Oedema of the palate is a later symptom. As late symptoms, enlargement of the cervical glands and imperfect closure of the jaw are common.

**Diagnosis** depends upon the fact that only a lesion of the lateral pharyngeal wall could give rise to this combination of symptoms: deafness of eustachian type, neuralgia of inferior maxillary division distribution, and defective mobility of the soft palate. Digital examination usually confirms the diagnosis.

Owing to late diagnosis, Trotter has not been able to obtain by operation a longer period of freedom from remission of symptoms than fifteen months.

In a recent paper, Jacod, who is assistant in the laryngological clinic of Professor Lannois at Lyon, describes a symptom-complex produced by growths in this region of the pharyngeal wall. In his cases the tumour spread upward through the foramen lacerum into the cranial cavity and produced deafness of eustachian tube type, fifth-nerve neuralgia, and paralysis of the optic, oculomotor, trochlear, and abducens nerves.

There seems little doubt that Jacod is describing the same type of growth as that recorded earlier by Trotter, though the paralyses in Jacod's cases are more extensive and seem to indicate either a terminal stage of the condition, or more pronounced upward extension into the skull. When the growth spreads up beside the body of the sphenoid we should expect the optic nerve and the nerves lying in the cavernous sinus to be affected, while it is easy to see that the seventh and eighth nerves, lying below the tentorium would escape. Jacod's first published series were recorded in 1914, and since this time he has seen seven fresh cases, the symptomatology of which he reviews in his present paper. F. M. R. W.

**Baudoin, C. Suggestion and auto-suggestion.** Trans. from the French by E. and C. Paul. *George Allen & Unwin, London,* 1920.

Thoughout the period of the Freudian upheaval the Nancy school has continued to work in its own special province of suggestion, and it has not been disturbed in the pursuit of its own views by the revolutionary views of Vienna. It has not denied their truth, rather it has congratulated the Freudians that their findings coincide so well with its own; but it has not thought that the new methods are of much value in practice, though of undoubted theoretical interest. In this book Dr. Baudoin has described the developments of the Nancy school, especially as they have been elaborated by his friend and colleague Dr. Émile Coué.

'There is no hypnotism, only suggestion,' said Bernheim. 'There is no suggestion, only auto-suggestion,' is the new dictum. 'Suggestion is the subconscious realization of the idea.' The meaning of this sentence is the theme of Dr. Baudoin's book. The realization of the idea is subconscious. This implies that it has nothing to do with will; indeed, the operation of will is worse than useless if it comes into conflict with an opposing idea charged with emotional tone. The will is always defeated by the idea. When we are learning to ride a bicycle we see a stone in the road; we try to avoid it and we collide with it. What has happened? The idea that we shall strike it has occurred, and this idea has been charged with the emotion of fear. To this we have opposed our will and assuredly it has not helped us. Now this is very curious. The road may have been twenty feet wide, the stone an inch or two. To have hit it fortuitously was unlikely, but we did hit it. The idea that we should do so was conscious, but the mechanism by which the idea was realized was concealed, was subconscious; and if the hitting was not fortuitous it must be a very accurate and perfect mechanism which produced such a result. The will not only failed to help us, but, such is the teaching, the more it was called into play, the more certain would we be to hit the stone. This phenomenon of the worse than useless effect of the will is called **the law of reversed effort.** 'So long as the imagination is adverse, so long as a counter-suggestion is at work, effort of the conscious will acts by contraries.' 'When the will and the imagination are at war, the imagination *invariably* wins the day.'

The idea which should have filled the tyro's mind was that the road was wide and the stone small, and that it would be really difficult for so poor a rider to hit it. These thoughts would certainly have been true, and the beginner was as free to consider them as those which he actually did entertain. The importance of this in psychotherapy is obvious. The insomnic lies awake because he is possessed with the idea that he will not sleep, and this idea is charged with the fear of what will happen if he does not. The more he tries to go to sleep, the wider awake does he become. The man who cannot concentrate believes that for him it is impossible, and all his conscious efforts result only in further wandering from his subject. The task of the physician is to bring the attention of the patient to the opposite idea, and to teach him how to hold it there. This is most easily and most profitably done in times of bodily and mental relaxation; for then the will is most in abeyance, and then contact with the subconscious is most easily obtained. That a method of this kind will cure a large number of the neuroses is certain. It has been well established that the expectation of symptoms is a fruitful cause of symptoms, but the claim here is that not only will this procedure cure those common manifestations which used to be called neurasthenic, but that the graver obsessional and compulsive cases are also restored to health by its employment. On this point it is difficult to give an opinion, but the question should certainly be investigated. Psycho-analysis is not regarded even by its devotees as a sure remedy for these conditions; and, if it were, something much shorter must be found if more than a small percentage of neuropaths are to be relieved.

The Nancy school goes still farther, and says that success has followed in certain cases of intractable organic disease, such as chronic eczema and varicose ulcer. We know that the regulation of internal secretions and of blood-supply is affected by the emotions, and it is therefore not impossible that emotional thought can alter the course of organic disease. This is a hard thought to many, but the subject should be approached with an open mind. The line between functional and organic is vague; who shall say where the possibilities of psychotherapy must end?

T. A. R.

**Brown, W. Psychology and psychotherapy.** *London, Edward Arnold,* 1920.

In this book of about two hundred pages, Dr. Brown gives the impression of having attempted to cover too much ground; and what he has written lacks proportion and plan. It hardly seems necessary in a little book on psychology and psychotherapy to enter the unknowable land of the relation of mind to brain, and in some twenty pages the subject has been compressed to the point of being unintelligible. Thus, 'If we explain consciousness in terms of brain change we are also explaining intellectual processes, which are a part of consciousness, in this way. That is to say, we are explaining consciousness in terms of something which needs consciousness for its explanation.' As the sentences stand, surely we are only explaining intellectual processes in terms of brain change. It may be that Dr. Brown regards it as an objection to the materialistic view that we need consciousness to understand consciousness, but that objection must apply to any theory of consciousness. Whatever may be the meaning of the sentences quoted, they need much amplification to bring it out. In a later part of the argument, it is curious to find the statement that the materialistic view wipes out the possibility of survival after death. Psychology has nothing to do with such a subject.

The clinical part of the work is occupied almost exclusively with war cases, and though he was very successful in abolishing hysterical symptoms taken in hand at an early stage, Dr. Brown seems to have been too easily satisfied in his delayed cases with immediate results, and too readily satisfied with odd explanations. He records a case, already described by him elsewhere, which he must therefore deem important, where a young man had loss of orientation so that when he was in a 'bus which turned through a right angle, he felt as though it had continued in a straight line. By an analytic investigation Dr. Brown arrived at a suppressed experience of a tumble in childhood, when the patient had fallen laterally to the ground

—that is, through a right angle. Shortly after this discovery the disorientation ceased; and in a brief interval the patient passed finally from observation. This case is described by Dr. Brown to illustrate therapy by hypnotic recovery of lost memories; and the more it is examined the less does it seem to illustrate anything at all.

Is there any human being who has not, at various periods of infancy and childhood, fallen through a right angle? Is a cure which has been observed for a few days only worth talking about?

Certain remarks made about soldiers after heavy fighting are unfortunate. Some of the men 'were keeping up with obvious effort rhythmical tremors which had no doubt been involuntary and irrepressible some hours before, but were now within the field of voluntary control. By distracting these cases with a rapid sequence of questions as to the origin of their disability, I was able to bring the tremors to an end.' The view is quite clear; because their tremors were brought to an end by distraction, they were voluntary. This is the view of the sergeant-major; it is also the view of a certain type of unimaginative doctor; it is an astounding view to come from a reader in psychology. If I am sad and a friend comes in and distracts me, does that imply that my sadness was voluntary and that I could have stopped it myself? Moreover, can rhythmic tremor be kept up *voluntarily* for any length of time?

On the whole, it must be said that the book is one of the many on psychotherapeutic subjects which had better not have been written. At the moment we are almost submerged beneath a flood of literature of this kind, disorderly both in thought and expression, and of no value. It is a pity that Dr. Brown has yielded to the impulse to add his quota to the muddy torrent. To the practitioner dealing with civilian cases the book will give no help; as a guide to modern psycho-pathology it is useless because of its compression and obscurity; as an epitome of general philosophy it is absurd. It is difficult to see for what class of reader it is intended.

T. A. R.

**André-Thomas.** Le réflexe pilomoteur. [**The pilomotor reflex.**] *Rev. neurol.*, 1920, **27**, 1139.

André-Thomas describes the receptive field, appropriate stimuli, and the characters of the response in this reflex under various conditions.

**In the normal subject** the pilomotor muscles may be excited directly by mechanical stimuli or reflexly. As a reflex it may be obtained by various stimuli applied to the skin, such as cold, friction, and the electric current. To unilateral stimuli the response is unilateral and may spread to the whole of the stimulated half of the body, or it may be restricted to one or more segmental areas. Certain cutaneous areas are particularly receptive, the nape of the neck and shoulders and the lower part of the axilla. When elicited from the neck the response is descending, and stronger stimuli are necessary to produce it over the head and neck. On the limbs, the extensor surfaces give the response more readily than the flexor surfaces. Bilateral stimuli produce a bilateral response.

**In lesions of the spinal cord** the response is exaggerated immediately below the upper level of the lesion. In total divisions of the cord, there are two forms of response: one above the level of the section, the 'réflexe encéphalique', and one below, the 'réflexe spinale'.

**The spinal reflex** in total divisions of the cord makes its appearance when the isolated portion of the cord emerges from spinal shock—that is, simultaneously with the mass reflex. It is elicited by the same stimuli as this reflex, namely, passive movements of the legs, &c. In these circumstances, the factors governing the distribution of the spinal reflex are the same as those governing that of the reflex sweating described by Head and Riddoch—that is, the distribution of the thoracico-lumbar white rami.

In partial lesions and in various diseases of the spinal cord, the response varies and is often difficult of interpretation. It is normal in poliomyelitis. In syringomyelia, variations in the response follow the distribution of vasomotor and trophic disturbances. In peripheral nerve lesions, the reflex response is abolished over the area of sensory changes, but, as Trotter and Davies showed, a local response to stimulation persists.

**The cerebral reflex**, that is, the response above the level of a cord lesion, varies greatly in facility and distribution. It descends to the level of the sympathetic distribution of the isolated portion of the cord.

In the normal subject the reflex is elicited by peripheral stimuli and also by various emotional states. The quality of the stimulus in both cases is similar and is strongly affective. In the former case, the sensations aroused by stimulation are of the affective variety and are unpleasant. Hence when the skin is anaesthetic no response can be obtained from it. The emotions producing the reflex are also unpleasant in quality. Fright and horror are the most adequate stimuli, but any profound emotion, whatever its quality, may be sufficient to produce it. The reflex of emotional origin is bilateral, that due to peripheral stimulation may be unilateral. The pilomotor reflex may therefore be regarded as an affective reflex.

F. M. R. W.

**Roussy, G.** Les lésions du corps thyroïde dans la maladie de Basedow. [**The thyroid lesions in Graves's disease.**] *Rev. neurol.*, 1920, **27**, 918.

Roussy distinguishes the following forms of Graves's disease: the common or essential form; secondary forms associated with infections of the thyroid (granulomatous or non-specific), with malignant disease, or with goitre in regions where goitre is common; and abortive forms of varying nature.

**The essential lesions** of the disease are found in the thyroid, thymus, and lymphatic glands. According to Roussy, the changes in the thyroid are characteristic and allow of diagnosis from microscopic examination alone. The features of the thyroid lesion are a parenchymatous hyperplasia affecting acini, epithelium, and colloid substance. The acini are smaller and more numerous than normal. Their form is irregular and the lumen may be absent. The cells are cubical and form intra-alveolar projections. Mitotic figures are rare, but desquamation is common. The colloid substance is diminished in amount, more fluid than normal, and stains feebly. Additional changes noted by Roussy and Clunet are clumps of eosinophil cells and of lymphocytes. The eosinophil clumps are found in about 50 per cent. of cases and are peculiar to this disease. The hyperplasia, though not characteristic in appearance, is so in its universal distribution throughout the affected gland.

A persistent or hypertrophied thymus is found in about 60 per cent. of cases, and proportional to this there may be enlargement of the lymphatic glands of neck, thorax, and abdomen.

The characteristic blood-changes consist in a leucopenia with a relative lymphocytosis, and a delayed coagulation time.

There are no constant lesions found elsewhere in viscera, glands, or nervous system. The sympathetic ganglia and trunks may show fatty infiltration and their cells degenerative and atrophic changes, but these changes are not constant or essential.

In long-standing cases various minor degrees of change may be found in various organs, but these are not constant and may be agonal changes.

**The pathogenesis of the disease.** While admitting that the sympathetic system probably plays a part in the symptomatology of the disease, Roussy thinks that this is not essential and is confined to the carriage of nervous impulses set up by toxic factors.

The various pluriglandular theories he dismisses as ingenious hypotheses without foundation. For him disordered thyroid function is the essential basis of the disease. He considers that dysthyroidism rather than hyperthyroidism is concerned. This would explain the association of symptoms of myxoedema and of Graves's disease in a single patient, and the fact that extract from the thyroid in Graves's disease may be less active than that from a normal gland. The relation of the thymus to the thyroid lesion remains obscure. In conclusion, Roussy would sum up as follows: that Graves's disease probably arises from an unnoticed inflammatory lesion of the thyroid and perhaps of the thymus also, which is followed by thyroid 'dyshyperplasia' and the production of an excessive and perverted secretion, which has a selective toxic action on certain organs or parts of the nervous system.

Of methods of **treatment**, Roussy considers radiotherapy the most efficacious, while the estimation of the **basal metabolism** is an important method of estimating the degree of thyroid activity and of controlling treatment.

From his own extensive observations during the war, Roussy does not believe that Graves's disease follows emotional disturbance or shock.

This abstract is taken from a report of a paper by Roussy read at the 24th annual congress of alienists and neurologists of French-speaking countries, held at Strasbourg during August 1920. At the end of the paper, the discussion which followed it is very briefly reported.

F. M. R. W.

**Westphal, A.** Über seltene motorische Erscheinungen bei multipler Sklerose, nebst Bemerkungen zur Differentialdiagnose gegenüber der Encephalitis epidemica. [**Unusual motor symptoms in disseminated sclerosis, with reference to the differential diagnosis from epidemic encephalitis.**] *Deutsche Ztschr. f. Nervenheilk.*, 1921, **68–9**, 128.

Westphal records three cases of disseminated sclerosis, two of which were confirmed by autopsy, in which unusual motor symptoms occurred suggesting the presence of encephalitis.

(1) A man of 35, who came under observation with widespread choreiform movements of limbs, grimacing movements of the face, and general restlessness. Speech was unintelligible, and standing and walking were impossible on account of the persistent involuntary movements. The

tendon-jerks were increased, the abdominal reflexes absent, and the plantar responses both extensor. It was not possible to determine the condition of the fundus oculi, nor the presence of nystagmus. The involuntary movement persisted during rest, but was grossly aggravated during movement, so that co-ordinated movement was impossible. During the six weeks before the patient died, the general unrest steadily increased. Speech remained practically unintelligible. The patient's mental state appeared normal, and he was perfectly oriented. It appeared that he had been ailing for three years. The picture was one of severe chorea with signs of pyramidal tract lesion. Examination of the brain revealed the characteristic lesions of disseminated sclerosis in great number involving all parts of the brain. Many of the foci were quite recent and their association with the blood-vessels was noteworthy.

(2) An unmarried woman of 23. For some years the menses had become irregular and she had lost practically all her hair, becoming bald. Her present illness dated back two years and had begun with involuntary movements in the legs following an air raid over Cologne in 1917. Soon walking became impossible and a tremor appeared in the left arm, and in head and trunk. Her mental state gradually deteriorated, but her hair had returned during these two years and she had become enormously fat. On examination, there were seen clonic flexion-extension movements of both lower limbs and in the left arm. She was unable to sit up, stand, or walk. The musculature of the right arm and of the face were alone unaffected. There was no paralysis. Both knee- and ankle-jerks were absent, the abdominal reflexes were absent, and the right plantar reflex was extensor. The left was unobtainable. There was nystagmus and she was incontinent of urine. Mentally, she was euphoric and fatuous. The clonic movements of the limbs increased under the influence of emotion. The pupil reactions varied from time to time from a good light reaction to complete immobility.

While under observation her speech became slow, and temporal pallor of the optic disks developed. Finally, contracture of the legs developed, she became emaciated, and died.

Autopsy revealed the presence of numerous focal lesions in the nervous system, of hydrocephalus, and of atrophy of the optic thalami. Microscopically, typical lesions of disseminated sclerosis were found, most abundant in the basal ganglia, cerebellar cortex, dentate nuclei, and posterior columns of the cord. Many of them were recent.

The clinical picture was one of dystrophia adiposo-genitalis with myoclonic symptoms and pyramidal signs.

(3) A man of 29, with a very recent history of contractions in the left leg. Examination revealed tonic spasms of the flexors and dorsiflexors of the leg and toes. These spasms were of varying duration and came on at frequent intervals, affecting different muscles in different attacks. The patient walked with the affected leg partly flexed and with foot and hallux strongly dorsiflexed. Occasionally the spasm was purely clonic. The plantar response on this side was extensor in type. The abdominal reflexes were present on both sides, the pupil reactions normal, and there was no squint, though there was a history of transient diplopia. There was abnormal pallor of the disks, but no defect of vision. The Wassermann reaction in the blood was negative. The illness began in 1919, and during 1920 the spasm described disappeared finally, to give place to fresh motor

symptoms. Athetotic movements appeared in the left arm. These developed from a slow mobile spasm to a wild jactitation of the limb accompanied by severe pain locally in the course of a few months. He was given a series of doses of silver-salvarsan totalling 5·0 grm. and improved considerably. His present condition is that there are no signs of pyramidal tract lesion, no sphincter disturbance, no sensory changes. The optic disks remain unchanged, and there is some nystagmus. Some movement of the left arm persists.

These three cases were all observed during the course of an outbreak of epidemic encephalitis. F. M. R. W.

**Nonne, M.** Zur Klinik der Myelomerkrankung der Wirbelsäule. [**Myeloma of the spine.**] *Neurol. Centralbl.*, 1921, **40**, 2.

Nonne gives a short review of the principal observations on this condition and a summary of the clinical picture. He describes a case in which a myelomatous nodule in the first thoracic vertebra gave rise to peculiar nervous symptoms. The patient was a man of 57, who came under observation for pains in the neck and arms, and for progressive wasting and pallor. A first examination revealed nothing but tenderness of the lower cervical and upper thoracic spine, albuminuria, and anaemia. He was admitted to hospital and four days later developed retention of urine. At this time there was marked tenderness of the lower cervical spine, a slight angular curve, and wasting of the ulnar muscles of the right arm and general weakness of this limb. Priapism and cyanosis of the penis appeared, myosis and loss of light reaction in the pupils, and then generalized cyanosis of the face, lip, and extremities. The cerebrospinal fluid was practically normal, and X-ray examination revealed rarefaction of the first thoracic vertebra. He died six days after admission to hospital. The diagnosis made during life was meningo-myelitis of the cervical cord of unknown origin.

At autopsy, the first thoracic vertebra was practically completely replaced by myeloma, which, however, did not project into the spinal canal. There were multiple myelomata in spine, ribs, and sternum. To the naked eye and microscopically the spinal cord and meninges were normal. The priapism remained after death.

Myosis and priapism are known to occur in lesions of the first dorsal and lower cervical segments of the cord. Nonne recalls observations in which so-called toxic nervous symptoms have been described in the nervous system as occurring in the course of cases of malignant disease in various parts of the body (Oppenheim, Bruns, &c.), and he concludes that the nervous symptoms in his case are of this nature. Although myeloma may not be malignant in the same sense as carcinoma, yet its course is invariably fatal, and he suggests that the appearance of nervous symptoms related to neighbouring segments of the cord in association with myeloma of the first dorsal vertebra may be regarded as evidence of malignancy in myeloma.

F. M. R. W.

**Lecène, P., et Lhermitte, J.** Une observation anatomo-clinique d'un cas de ramollissement cérébral consécutif à l'oblitération de l'artère sylvienne gauche par une embolie métallique. [**Cerebral softening from a metallic embolus in the left middle cerebral artery.**] *Rev. neurol.*, 1920, **27**, 1116.

The patient, a healthy soldier of 30 years, received multiple small shell wounds on August 31, 1918. Included among these was a small punctured wound below and behind the left angle of the jaw.

When observed on the same day the patient's grave condition was in striking contrast to the trivial nature of his external injuries. He was semi-conscious and had a rapid feeble pulse of 140 per minute. He answered questions by an inarticulate grunt, and the most that could be elicited from him was the repeated phrase 'fait mal'. There was no true paralysis, but slight rigidity of the right arm was noted.

On the following day he was unable to utter a word, there was complete aphasia. He appeared to comprehend what was said to him perfectly. The slight rigidity of the right arm noted earlier persisted, but did not interfere with voluntary movement of the limb. There were no local signs of a wound of the carotid artery.

On the third day (September 3) there was a complete right hemiplegia, with flaccidity of the paralysed limbs and loss of tendon-jerks on the right side. The right plantar response was of Babinski type. Complete aphasia remained.

On the three following days the patient's general condition grew steadily worse. He was somewhat delirious, the right hemiplegia persisted, the patient was speechless, but could close both eyes to order. He died on September 6.

Examination *post mortem* revealed lobar pneumonia of the right lung and a small punctured wound of the internal carotid on the left side just above its point of origin from the common carotid artery. The artery was normal elsewhere. The anterior cerebral artery and the circle of Willis were normal. On opening the left Sylvian fossa, a black speck became visible on the middle cerebral artery three centimetres from its junction with the circle of Willis. The artery was found to be completely occluded here by a small shell fragment. Distal to this, the artery and its branches were thrombosed. The other vessels were normal.

On horizontal section, the left centrum semi-ovale in its middle segment was softened and diffluent, livid in colour, with several haemorrhagic areas. The external part of the head of the caudate nucleus and the two external segments of the lenticular nucleus were also softened and bluish in colour. The external medullary lamina and the external capsule were not recognizable, being replaced by a cavity. The insula and all the cerebral convolutions were normal. The thalamus appeared normal.

Microscopically, the frontal convolutions were normal both as regards blood-vessels and cells. The Rolandic convolutions showed no vascular lesion, but the cells of Betz were in a state of chromatolysis. There was some oedema of the cortex of the insula and some diapedesis round the vessels. In short, the cortex was relatively little altered. The thalamus was also virtually intact, and, beyond excess of lipoid granules in the cells, was normal.

The caudate nucleus was altered throughout its whole extent. Numerous veins were thrombosed, there was haemorrhage from the capillaries, and the nerve-cells were grossly degenerated. The putamen was completely necrosed and its vessels thrombosed. In the external segment of the globus pallidus there were numerous capillary haemorrhages and oedema. The nerve-cells were relatively intact.

In the internal capsule the fibres were separated by oedema, but were otherwise normal. Numerous compound granular corpuscles were seen here.

In their commentary on the case, Lecéne and Lhermitte note the initial absence of localizing symptoms, then the appearance of complete aphasia without signs of hemiplegia except for the trivial change in tone in the muscles of the right arm for twenty-four hours. Not less striking was the absence of definite evidence of a wound of the internal carotid artery in the neck. The severity of the general cerebral symptoms, the rapid development of aphasia, hemiplegia, and death from a small metallic embolus, the entry of which was missed during life, suggest that some at least of the fatal cases said to be due to shell explosion without wound may have a similar origin.

According to the authors, it is in connexion with the question of the cerebral arterial supply that the case has its greatest interest. Contrary to what some observers have stated, the cerebral cortex obtains its blood-supply from a network in the pia formed by branches of all three cerebral arteries. So free is the anastomosis between the branches arising from the three parent arteries, that obliteration of one of these scarcely affects the blood-flow through the network. If, as in a young subject, the vessels are healthy, obliteration of one of them does not lead to an appreciable lesion of the cortex. This is well seen in the case here recorded. The basal arteries, on the other hand, are strictly terminal. They arise from all three cerebral arteries and from the anterior choroid and communicating arteries. Blocking of a single set, such as those arising from the middle cerebral artery, should give rise to a well-defined area of softening.

After shortly reviewing the various statements as to the blood-supply of the basal ganglia (Beevor, Heubner, Charpy), the authors point out that in their case, from blocking of the basal vessels arising from the middle cerebral artery, there resulted softening and complete necrosis of the putamen, external segment of globus pallidus, and of head and middle part of caudate nucleus. The internal capsule was merely oedematous and contained numerous granular corpuscles, and the thalamus was intact. In short, the middle segment of the centrum semi-ovale was necrosed, and on this lesion the hemiplegia depended. F. M. R. W.

**Dide** et **Guiraud**. Procédé électif de coloration des granulations lipoïdes cellulaires dans les centres nerveux. [**Special staining method for lipoid granules in nerve-cells.**] *Rev. neurol.*, 1920, **27**, 1124.

The method is applicable to alcohol or formalin fixed tissue in paraffin sections.

(1) Stain for a minute in a freshly prepared solution of methyl-violet grms. 0·5 in 100 c.c. of anilin water.

(2) Then fix for a minute in a solution of iodine grms. 5·0, potassium iodide gms. 5·0 in 150 c.c. of distilled water.

(3) Decolorize in 90 per cent. alcohol, and then in acetone until no more blue or iodine comes away from the section.

(4) Wash in distilled water.

(5) Counterstain in 0·5 per cent. eosin solution.

(6) Dehydrate and mount in neutral balsam.

Myelinated fibres stain pale violet; nerve-cells rose with pale violet nucleus and blue-violet nucleolus; lipoid granules in cells and in vessel-walls and neuroglia nuclei stain an intense blue.

The colouring is said to be permanent. F. M. R. W.

**HARBITZ, F. 'Encephalitis' neonatorum.** *Norsk. Mag. f. Lægevidensk.*, 1921, **82**, 25-30.

Harbitz describes as a pathological curiosity a case of a child which survived birth only by about 14 hours. It was in about the thirtieth week, and the mother, who was a married woman with one child, suffering from albuminuria and pyuria. The infant showed no sign of syphilis, but the liver was cirrhotic, the kidneys showed doubtful signs of nephritis, and there were haemorrhages in the skin, kidneys, and peritoneum, as well as a considerable haemorrhage of the meninges, originating in all probability from an aneurysm of an artery in the Sylvian fossa. In addition to jaundice and ascites, internal hydrocephalus was found; and scattered throughout the central ganglia and the cortex of the cerebrum were large, greyish-white and yellow necrotic patches which were partially calcified. Small granules of fat were grouped round the blood-vessels of the brain. Harbitz, who is professor of morbid anatomy in Christiania, confesses to ignorance of the aetiology of this condition. The internal hydrocephalus was evidently secondary to this condition, which is undoubtedly more common among the new-born than is generally supposed, and which Harbitz gives the comparatively non-committal label 'encephalitis'. C. L.

**LINDBERG, G.** Om posttraumatisk serös meningit hos barn. [**Post-traumatic serous meningitis in children.**] *Hygeia*, 1921, **83**, 15-24.

Lindberg suspects that serous meningitis is a comparatively common condition in children as a sequel to injuries to the head. Yet the published accounts of such cases are scanty—a fact traceable to the infrequency with which lumbar puncture is undertaken. Lindberg records two cases. One was that of a boy, aged 10, who fell on the back of his head as he was playing. The slight abrasion was ignored, but a couple of days later he developed headache and general hyperaesthesia. Later he became drowsy and very sensitive to sound. The headache became more severe, but he did not vomit. On examination he presented the characteristic signs of severe meningitis, and the case would have been dismissed as one of tuberculous meningitis but for the history of a fall. Lumbar puncture revealed a pressure of 200 mm. and yielded 15 c.cm. of perfectly clear fluid, in the sediment of which were only a few lymphocytes. Nonne's and Boveri's potassium permanganate reactions were negative. When lumbar puncture was repeated some time later, the pressure had fallen to 180 mm. Improvement rapidly followed, and though the boy was forgetful for some time, he ultimately recovered completely. In the second case the cerebrospinal fluid was under as high a pressure as 300 mm. The withdrawal of 20 c.cm. effected an even more dramatic improvement than in the first case. This patient also recovered completely, and Lindberg is inclined to attribute both recoveries to the relief of pressure effected by lumbar puncture. It is impossible to say what the prognosis is in such cases in the absence of lumbar puncture,

for by this alone can the correct diagnosis be made. Lindberg's paper is, in short, a plea for lumbar puncture in every case with signs of meningitis.
C. L.

**Lindstedt, F. Contribution to the pathogenesis of sciatica.** *Acta Med. Scand.*, 1921, **53**, 733–7.

Lindstedt has examined a series of cases of sciatica, diagnosed as such by others than himself in the principal hospitals in Stockholm. Among 100 consecutive cases he found as many as 91 which presented static changes of various kinds. Serious diseases of the knee were found in 14 cases, a history of rheumatic arthritis in 12, hip disease in 11, varicose veins in 8, affections of the spine, such as spondylitis deformans, fracture, &c., in 8, and pronounced flat-foot in another 8. In 5 cases there were pronounced traumatic injuries to the foot, and in 4 a high degree of relaxation of the ligaments of the knee associated with genu recurvatum. In as many as 7 cases the complications of sciatica were of gonorrhoeal origin. Lindstedt supplements these facts with the following comments: The diagnosis of sciatica having been made by various hospital physicians, not by himself, the objection could not be raised that his cases were in any sense picked. Most of the complications detected were serious and conspicuous; their coexistence with the sciatica could not be merely accidental, for the occurrence of affections of the knees, of polyarthritis, varicose veins, and flat-foot was too frequent to be explained away thus. Indeed, some of these complications were of a relatively rare kind. Again, when they were unilateral, they were invariably on the same side as the sciatica. Lindstedt concludes that sciatica is often an irradiating, reflected neuralgia, analogous to the trigeminal neuralgia following presbyopia or toothache. C. L.

**Schmidt, V.** 100 Tilfælde af Recurrensparese. [**100 cases of paralysis of the recurrent laryngeal nerve.**] *Hosp.-Tid.*, 1921, **64**, 17–21.

Schmidt has examined the records of 85 cases of paralysis of the recurrent laryngeal nerve treated at the Rigshospital in Copenhagen, and of 15 similar cases at another hospital. He tabulates these cases so as to show the comparative frequency of the different causes, the sex incidence and the comparative number of right- and left-sided cases. As for the age incidence, when the bulbar, post-infectious, and traumatic cases under the age of 3 years were excluded, it was found that there was a steady rise from 35 to 60. After this age there was an equally steady decline. In about 60 cases the cause of the paralysis was located below the upper aperture of the thorax. In 45 cases carcinoma or sarcoma was responsible. In 9 of the 13 cases of aneurysm of the aorta, the patients were men, and several of them had complained of hoarseness before suffering from any marked cardiac discomfort. As curiosities, 2 cases are mentioned in which heart disease provoked paralysis of the right recurrent nerve. All the 9 cases of new growths in the neck gave rise to right-sided paralysis, an observation which Schmidt correlates with the comparatively exposed course of the nerve on the right side. He concludes that to diagnose paralysis of the recurrent nerve and then to lose sight of the patient is unpardonable. C. L.

# PATHOLOGY AND BACTERIOLOGY

**Evans, C. Lovatt. On a probable error in determinations by means of the hydrogen electrode.** *J. Physiol.*, 1921, **54**, 353.

The results of determinations of the hydrogen-ion concentration of the blood by the colorimetric method recommended by Dale and Evans are not in agreement with those of other observers who employed the electrometric method. The values obtained by the former method are approximately $P_H$ 0·2 higher than those given by the hydrogen electrode, or by calculations based on constants derived from electrode determinations. The reason for the discrepancy being obscure, the author has sought to compare directly the two methods to find under what conditions it appeared. The calculated reaction of a bicarbonate solution agrees with that determined colorimetrically if values for the degree of ionization of the bicarbonate ($\delta$) and the apparent dissociation constant of carbonic acid ($k$) as determined by the conductivity method are employed. If the constants $k$ or $\delta$ derived from hydrogen electrode measurements are used in calculating the reaction of a bicarbonate solution, the results agree naturally with those of direct observation by means of the hydrogen electrode, because in such a calculation $k$ is larger or $\delta$ smaller than is found by the conductivity method. Such calculated results obviously do not agree with colorimetric determinations. It is inferred that it is the hydrogen electrode determinations and not the colorimetric ones which are erroneous in these cases. A source of error in the hydrogen electrode is indicated in that formic acid is produced by catalysis when the solution in the hydrogen electrode contains carbonates.

W. A. M. S.

**Heymans, J. Y.** *In vivo* comme *in vitro* les microbes passent à travers la paroi du filtre. [***In vivo* as *in vitro* bacteria pass through the walls of filters.**] *Compt. rend. Acad. d. Sc.*, 1920, **171**, 971.

During his attempts at antituberculous vaccination by means of virulent bacilli enclosed in a 'sac de roseau', the author had observed that after a certain time the bacilli were found outside the sac. This observation led him to make experiments *in vitro*, the conclusion of which was that if bouillon cultures of bacteria are introduced into a filter ('sacs de roseau', collodion capsules, Pasteur filter-candles, parchment filters, 'ultra-filtres') the bacteria always pass from the interior of the filter into the surrounding medium (see *Arch. internat. de pharmacodyn. et de thérap.*, 1912, **22**, 49). Though aware that the presence in the wall of the filters of even one minute pore of about the same diameter as that of the bacteria experimented with would have been sufficient to explain the results of his experiments, the author puts forward the suggestion that bacteria may pass through the wall of filters by pores smaller than their size, owing to their capacity for squeezing themselves into ultra-microscopic sizes, in a manner comparable to the diapedesis of leucocytes.

With the object of obtaining further evidence in support of this view, the author has now made a new series of experiments, using spores of *B. anthracis*. These were introduced by means of threads into 'sacs de roseau' previously tested and containing 0·05 gr. of dried potato powder. After having tightly tied and collodionized the ends of the sacs, the latter were enclosed in gelatin capsules and finally placed in the peritoneal cavity of rabbits. Within two or three days all of them died of anthrax. The author then made a new set of experiments by means of 'sacs de roseau' prepared as before, but dipped 5, 10, up to even 20 times into fluid collodion, so that before being enclosed in the gelatin capsules and introduced into the peritoneal cavity of rabbits, the sacs were coated with a membrane of collodion many layers thick. The rabbits survived for longer periods of 5, 10, or 15 days, but in the end they all died of generalized anthrax. The author then made another set of experiments, using flexible instead of simple collodion and repeating the operations of dipping the sacs into it, and allowing the successive layers of collodion to dry as many as thirty times. The rabbits survived for still longer periods than in the other experiments, but even in this case they all died of generalized anthrax.

After having considered all possible explanations, the author comes to the conclusion that, as *in vitro*, so also *in vivo*, bacteria (in this case spores of *B. anthracis*) may germinate and pass through pores of apparently continuous membranes in the form of extremely minute or ultra-microscopic bodies, their size being about that which is characteristic of the so-called invisible or filter-passing germs. C. d. F.

**Nicolle, C.**, et **Conseil, E.** Vaccination préventive de l'homme contre la fièvre méditerranéenne. [**Prophylactic vaccination against Malta fever.**] *Compt. rend. Acad. d. sc.*, 1920, **171**, 775.

Three natives of Tunis (who do not drink goat's milk, and rarely suffer from Malta fever) were the subjects experimented on. The two who had been vaccinated with dead cultures of *M. melitensis* failed to develop the disease on receiving a subcutaneous injection of the living organism. The third one, who acted as control and had not been vaccinated, developed the disease on the eighteenth day after receiving a subcutaneous injection of the living organism. Agglutinins appeared in the blood-serum of the latter two days before the onset of pyrexia and rapidly increased in titre. No agglutinins could be demonstrated in the blood-serum of the other two.

Nicolle and Conseil advise the use of such vaccination for laboratory workers on account of the frequency of accidental infection amongst them. They also point to this experiment as an instance of the statement that the presence of agglutinins indicates infection and not immunization.

J. R. P.

**Barnes, W. H.** **The activity of staphylococci in milk.** *J. Infect. Dis.*, 1921, **28**, 259.

A study of the changes induced when staphylococci are grown in milk. The author found five different types of action among 180 cultures examined, and believes that milk is a valuable medium for distinguishing staphylococci which otherwise may appear to be alike. W. B.

**Rockwell, G. E.**, and **McKhann, C. F.** **The growth of gonococcus in various gaseous environments.** *J. Infect. Dis.*, 1921, **28**, 249.

In 1916 Wherry and Oliver claimed that, when first isolated, the gonococcus grows best under the partial tension produced by *B. subtilis.*

The present authors have studied this question with more exact methods, and find that cultures of gonococcus isolated at partial tension by the aid of *B. subtilis* grow under pure hydrogen, but not under carbon dioxide or oxygen. Anaerobic conditions induced by caustic soda and pyrogallic acid were, however, deleterious. In the continuous cultivation of gonococcus under various gases the viability was greatest under hydrogen and least under oxygen. W. B.

**Hermanies, J. Gonococcus types.** *J. Infect. Dis.*, 1921, **28**, 133.

On the basis of the examination of a large number of strains of gonococci, the author confirms the general experience that by absorption tests there are immunological types which have very little relation to each other. The agglutinins of a serum evoked from one type of gonococcus cannot be absorbed by any of the strains forming the other types.

W. B.

**Kraft, Ad. Hemolytic streptococci of the appendix vermiformis.** *J. Infect. Dis.*, 1921, **28**, 122.

This is a contribution to the question of the significance of haemolytic streptococci in the aetiology of appendicitis. Altogether, the author examined 175 appendixes, special attention being directed to 48 normal specimens and 77 pathological. In the normal series haemolytic streptococci were found in 2 (4·17 per cent.) whereas in the pathological specimens they were found in 4 (5·2 per cent.), and then only in the acute cases. When they were found in pathological specimens they were present in such numbers as to suggest almost a pure culture. The author, however, concludes that they did not play an important part in the aetiology of the disease. W. B.

**Dible, J. H. The enterococcus and the faecal streptococci: their properties and relations.** *J. Path. & Bacteriol.*, 1921, **24**, 3.

The author points out that streptococcus-like organisms in the faeces have been the subject of very numerous descriptions, and that many of the types described should be disregarded in the light of more modern work. There appear, however, to be certain constantly recurring types which are more or less distinct. Of these he considers the following three groups as worthy of critical consideration:

1. The enterococcus of Thiercelin.
2. The *Streptococcus enteritis* (Hirsh and Libman).
3. The *Streptococcus faecalis* of Andrewes and Horder.

After describing the characteristics of these organisms as recorded by various workers, he points out that while descriptions of *Streptococcus faecalis* are all comparable these differ widely from descriptions of the enterococcus, and further, descriptions of the latter differ considerably among themselves. The paper under review is based on the study of 152 strains of streptococci isolated from faeces partly in the ordinary routine of laboratory work and partly in a special examination of individual stools.

The following properties were studied:

Morphology; biological properties: fermentative ability, growth on gelatin at 22° C., haemolysis, bile solubility, pathogenicity, and thermoresistance.

It was found that with three exceptions all had saccharolytic properties. A complete table of these is given.

Haemolysis occurred with two strains only. A certain degree of pathogenicity was shown by 13 strains only.

The bile solubility test was invariably negative. With regard to heat resistance it was found that they fell into two groups. The property of heat resistance or its absence was then taken and the association between this property and ability to ferment raffinose or mannite, and chain formation is shown in a table together with the corresponding theoretical figures calculated on the assumption of complete independence.

The degree of definite association of properties is shown by the use of Yule's coefficients of association. It is shown that the association of heat resistance with mannite fermentation and its negative association with chain production and raffinose fermentation are well marked. The results lead to the finding of two main groups:

1. Those showing properties of fermenting mannite, resisting heat, and forming diplococci. These are considered to come under the names *Enterococcus* and *Streptococcus faecalis.*
2. Those which do not ferment mannite or resist heat and tend to chain or conglomerate formation. This group includes *Streptococcus salivarius* and *S. mitis* and as variants *Streptococcus pyogenes* and pneumococcus.

The author concludes from his investigations that the group of *Streptococcus enteritis* comprises many forms which are surviving salivary types.

The *Streptococcus faecalis* of Andrewes and Horder comprised the group of the enterococcus, but omit many true enterococci by not recognizing non-mannitol-fermenting variants. G. T. W.

**Thomsen, O., u. Wulff, F.** Nogle Problemer vedrörende Meningococinfektionen. [**Certain problems concerning meningococcal infection.**] *Hosp.-Tid.*, 1921, **64**, 17–28, 33–45.

Thomsen and Wulff describe a small epidemic of cerebrospinal meningitis in a draft of 275 recruits lodged in barracks. Soon after the outbreak, every soldier was examined for meningococci, and all the carriers of the virulent Type A were isolated. In addition to the 16 cases harbouring Type A there were 15 carriers of non-virulent meningococci. An instructive feature of the epidemic was the observation that on the east side of the barracks, which was comparatively dark and damp, there were 22 cases; on the west side there were only 9. Yet there were approximately as many men on one side as the other. The authors suggest that the unhygienic conditions of the east side of the barracks had lowered the resistance of the men on this side, and they note that army surgeons have often found cerebrospinal meningitis among soldiers to be practically confined to units lodged in dark and damp quarters.

In Denmark, all the recent cases of meningococcal sepsis, and about 90 per cent. of the cases of meningococcal meningitis, have been traced to the serologically well-defined Type A, which is quite distinct from the four pathogenic types identified in England. The virulence of meningococci, which are not toxin producers in the ordinary sense, depends on their rapid autolysis and the liberation of endotoxins. There may be some differences in the toxicity of the endotoxins of the various types and strains, but the importance of these differences is insignificant compared with the differences in their reproductive capacities.

As a working hypothesis, the concentration of antibodies naturally present in the nasopharyngeal secretions may be put at a third of the concentration of these antibodies in the blood. If persons are classified in three groups according to the concentration of antibodies in the blood and nasopharynx, then in Group I, with lowest concentration of antibodies, meningococci can multiply in both nasopharynx and blood, in Group II in nasopharynx alone, the person becoming a carrier, and in Group III neither in nasopharynx nor blood. Discussing the explanations hitherto given for the fact that recruits are much more susceptible to cerebrospinal meningitis than older drafts, the authors dismiss these explanations as unconvincing. For example, the explanation that susceptible persons are weeded out by developing the disease while they are raw recruits does not account for the numerous instances of immunity shown by older drafts which, in their recruit stage, were not involved in a meningococcal epidemic. Though no weeding out of 'susceptibles' among these older drafts has occurred, they prove immune to an epidemic among recruits in their midst.

Among 163 trained soldiers systematically examined for meningococci, 55 (34 per cent.) proved to be carriers, Type A being found in 25. As there was no case of cerebrospinal meningitis, none of these 25 carriers was isolated. But a month after this draft had been diluted with recruits several of the latter fell ill. The authors attach much importance to the mutual antagonism of the different types of meningococcus, and they believe that when one type has established itself in the nasopharynx, other types cannot secure a footing. Consequently a Group I person, with the lowest concentration of natural antibodies, may be immune to virulent meningococci because he is a carrier of an avirulent type. One of the two following sequences may occur:

1. Recruits join trained soldiers among whom there are no carriers of Type A, but only carriers of avirulent types. In a few months these avirulent types will, under the overcrowded conditions of military service, spread to the nasopharynx of every Group I person among the recruits. If now carriers of Type A are introduced, these Group I persons will be protected by their avirulent meningococci; Group II persons will resist blood infection by Type A because of their comparatively high concentration of natural antibodies, but will become carriers of Type A; and Group III persons will neither fall ill of, nor become carriers of, Type A. Or:

2. Recruits join trained soldiers among whom are carriers of Type A. Group I persons among the recruits, not having had time to cultivate avirulent meningococci, are infected by Type A and fall ill. There is also the possibility that a Group I person may cease to harbour avirulent meningococci, and he then succumbs to Type A. This explanation might account for the case of a trained soldier who, as occasionally happens, falls ill even after long service.

Applying their hypotheses to the observations of Gordon and his associates, the authors reproduce the chart (*M.R.C. Special Report Series* 50. J. A. Glover, p. 141) showing the ratio of inagglutinable to epidemic strains from time to time, and they suggest that the 'warning rise' in the number of carriers of avirulent, inagglutinable strains is simply the effect of overcrowding. Such overcrowding has, however, no ill effect till virulent meningococci are introduced and newcomers, unprotected by non-virulent strains, join the draft. The authors' hypotheses may also account for differences in the epidemiology of the disease (*a*) in crowded barracks and (*b*) in areas where soldiers are billeted in twos or threes. In the latter case both protective cultivation of avirulent strains, and infection by virulent strains is comparatively irregular, and outbreaks of the disease are only sporadic.

The authors revise their views as to augmentation of virulence of meningococci by frequent passages. These, they now believe, cannot convert a non-virulent to a highly virulent meningococcus; one type cannot be converted into another, but it is probable that within the same type there may be changes of virulence, witness the frequent occurrence of petechial cases in Denmark since 1917. The alternative explanation—that the type causing petechiae did not exist in Denmark before 1917—is dismissed as improbable, for it implies that the type which existed before 1917, and which gave rise to cerebrospinal fever without petechiae, should have died out since 1917. Notifications of cerebrospinal fever in Denmark since 1910 showed a marked rise in 1916, but the petechial cases, which now constitute 50 to 60 per cent. of all cases, did not appear till 1917. Probably the numerical rise in 1916 was the first indication of a rise in virulence, and this rise culminated in 1917 with the appearance of petechial cases. The prophecy is made that this enhanced virulence of certain strains of Type A will not be maintained, and petechial cases will cease to occur.

After arguing that the carrier who does not fall ill within a day or two of infection is most unlikely to develop the disease because his natural immunity is progressively augmented by abortive invasions of the blood by the meningococcus, the authors recommend (1) that during the first months of their military service recruits should be kept apart as much as possible from older drafts; (2) that recruits should be given the most hygienic quarters in barracks in preference to older soldiers, and (3) that when these are selected as teachers for recruits they should first be examined for Type A meningococci, which, if present, should disqualify these older soldiers from teaching recruits. C. L.

**Vaudremer, A.** Un bacille tuberculeux humain, un bacille tuberculeux bovin, acidorésistants facultatifs. [**Facultative acid fastness in tubercle bacilli, human and bovine.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 259.

The author experimented with two strains of tubercle bacilli, the one human and the other bovine in type. Both were pathogenic for the guinea-pig and both produced tuberculin. By growing them for some weeks on 2 per cent. glucose agar (without glycerine) they lost their acid-fast character and became easily stained with gentian violet. On inoculation into guinea-pigs an abscess was produced, and the bacilli were found to have regained their acid-fastness. Inoculated into 2 per cent. peptone water the non-acid-fast bacilli grown at 38° C. for eight days produced an abundant culture with mycelial threads swollen at the ends. The acid-fastness could also be restored by culture on ordinary agar to which a trace of fresh serum had been added, or by inoculation on glycerine-containing media. W. B.

**Fürth.** Beitrag zur antigenen Wirkung von schwach virulenten Tuberkelbazillen, Schildkröten- und anderen säurefesten Bazillen. [**On the antigenic action of attenuated tubercle bacilli, tortoise, and other acid-fast bacilli.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **91**, 197.

A short series of experiments made to determine whether attenuated cultures of tubercle bacilli, grass bacilli, and Friedmann's tortoise bacilli are capable of acting as antigens. The result was determined by subsequent inoculation of tubercle bacilli. Normal guinea-pigs can withstand 100–150 mgr. of dead tubercle bacilli without harm, whereas those that have become hypersensitive become acutely ill and die within 24 hours. Using this test he found that Vallée's attenuated tubercle bacillus culture and a strain of fowl tubercle are antigenic, especially when administered in large doses. Acid-fast grass bacilli and Friedmann's bacillus have no such action, and differ entirely from tubercle bacilli in this respect. W. B.

**Alilaire, E.**, et **Fernbach, E.** Quelques observations sur la culture du bacille tuberculeux en milieu non glycériné. [**The cultivation of the tubercle bacillus in glycerine-free media.**] *Compt. rend. Acad. d. sc.*, 1920, **171**, 375.

By substituting a similar quantity of gum arabic for glycerine in glycerine broth (4 per cent.), A. and F. succeeded in obtaining an abundant growth of the tubercle bacillus.

An analysis of dried cultures, obtained from gum arabic broth and glycerine broth respectively, showed that the total nitrogen of the former was double that of the latter, but the fat content of the latter was four times that of the former. A. and F. suggest that its high fat content, which has so far placed the tubercle bacillus in a category of its own amongst bacteria, may be due to the fact that the cultures analysed were obtained from media containing glycerine. J. R. P.

**Henrici, A. T.**, and **Gardner, E. L.** **The acid-fast actinomycetes, with a report of a case from which a new species was isolated.** *J. Infect. Dis.*, 1921, **28**, 232.

A more or less detailed account of the 26 cases recorded, in the literature, of acid-fast actinomycetes, together with the report of a case the cultures from which resembled those described by Aoyama and Miyamoto and by Birt and Leishman in the white appearance of the growth on solid media. The authors' patient was a female, 31 years of age, who for three years had suffered from cough, expectoration, and weakness. The sputum showed numerous slightly acid-fast branched filaments. Inoculation of the sputum killed guinea-pigs in a few days with a nodular irruption, from which the fungus was easily obtained in a pure state. The special peculiarities of the organism were that it coagulated milk in an alkaline medium, digested the coagulated casein, rapidly liquefied gelatin, and darkened media containing peptone. The authors believe that the various species of acid-fast actinomycetes can be arranged in a fairly uniform series with Eppinger's variety at one end, establishing contact with the acid-fast bacteria, and their own strain at the opposite end, where it links up with the non-acid-fast actinomycetes. On account of the chalky-white appearance of the growth on solid media they propose the name of *Actinomyces gypsoides* for the new species. W. B.

**De Witt, Lydia M. Mercury compounds in the chemotherapy of experimental tuberculosis in guinea-pigs.** *J. Infect. Dis.*, 1921, **28**, 150.

This is an investigation into the chemotherapy of tuberculosis in the guinea-pig by a large number of mercury-containing compounds; many of which were specially prepared for the purpose of the research. The results in general were disappointing, although in comparison with untreated controls that had been inoculated with the same dose of the same strain of tubercle bacilli some of the animals treated with mercury compounds showed a prolongation of life and a diminished dissemination of the pathological lesions. It must be pointed out that in nearly all of these, however, the infection was one with a strain of low virulence. When the same drug was tested with a strain of high virulence no effect was noted. Only with one set of animals treated with the double salt of methylene blue and mercuric chloride, and with a set treated with diazoamino-methylene blue-o-phenol mercuric chloride, was there a beneficial effect in the case of guinea-pigs that had received a virulent strain of tubercle bacilli. In no case, however, was the disease cured. W. B.

**Kolmer, J. A., Davis, L. C.,** and **Jager, R. The influence of chaulmoogra oil on the tubercle bacillus.** *J. Infect. Dis.*, 1921, **28**, 265.

A series of experiments to determine the effect of chaulmoogra oil on a strain of bovine tubercle bacillus. The results were negative, for even the undiluted oil had no germicidal influence *in vitro* nor upon the infective properties of T. B. *in vivo*. In doses of 0·2 c.c. per 100 grm. of body-weight the oil had none or only a slight effect on experimental tuberculosis in infected guinea-pigs. W. B.

**Fineman, Bertha, C. A study of the thrush parasite.** *J. Infect. Dis.*, 1921, **28**, 185.

The thrush fungus, which was discovered by Berg in 1839, has been the subject of innumerable investigations,especially as regards its morphology and botanical position and the unity or plurality of species. From the study of 17 strains the authoress concludes that they agree in their morphological and cultural characters, carbohydrates being fermented uniformly and constantly. Agglutinins were not produced in quantities sufficient to be of diagnostic value. The fungus produces chlamydospores but not ascospores, and should be classified in the genus *Oidium*. It tends to assume mycelial forms in liquid media, in media containing complex carbohydrates, in media of low oxygen or surface tension, while the yeast-like form is met with particularly on solid media, in the presence of simple carbohydrates, an abundance of oxygen, or on media of higher surface tension. Apparently, the mycelial form develops in relatively unfavourable conditions. The paper contains a clear exposition of the different views that have been held on this common but complex organism. W. B.

**Levaditi, C.,** et **Harvier, P.** (1). Étude expérimentale de l'encéphalite dite léthargique. [**Experimental study on so-called encephalitis lethargica.**] *Ann. de l'Inst. Pasteur*, 1920, **34,** 911.

**Levaditi, C.**, et **Harvier, P.** (2). Recherches expérimentales sur l'encéphalite épidémique. [**Experimental researches on epidemic encephalitis.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 388.

Attention has already been called to the important researches of Levaditi and Harvier on encephalitis lethargica (*Medical Science*, 1920, **2**, 285, 411, 572, 1920–1, **3**, 460, 545, 1921, **4**, 148). The first of the present papers is a full account of their researches and contains many new details. They conclude that the virus of lethargic encephalitis is pathogenic for the guinea-pig and rabbit, but is only slightly so or actually non-pathogenic for the monkey. The lesions produced in susceptible animals are approximately the same as those found in man. By experiments they show that the virus traverses the Chamberland bougies Nos. 1 and 3, and is conserved in glycerine at the temperature of the ice-box for 19 days. Dried over sulphuric acid or potash at 22° C. the virus maintains its virulence for at least four days, but is destroyed at 55° C. Although the virus can survive a 1 per cent. solution of phenol for 15 minutes it is destroyed by prolonged contact with this antiseptic. After the death of an animal from encephalitis the virus is living and active up to 48 hours.

With regard to the experimental disease, transmission may be brought about by intracranial, intra-ocular, or intranerve inoculation, but not by injection under the skin or into the veins, peritoneum, trachea, alimentary canal, or into the salivary glands. Inoculation into the substance of the testicle provokes a fatal encephalitis, although the incubation period is prolonged. In the testicle the virus is preserved and may, perhaps, multiply for as long as 17 days, although no macroscopic or microscopic lesions are demonstrable. Apparently, the virus can traverse the nasal mucous membrane only when it is injured or inflamed. It then probably ascends to the brain by way of the olfactory nerves. The exit of the virus from the body is probably in the nasopharyngeal secretions, and the disease is transmitted by this medium and particularly by carriers. Spontaneous recovery does not occur in the experimentally produced disease. Immunity may, however, be produced experimentally by the virus, living or dead. The immunity is not absolute, but exists in a degree sufficient for study. The immunity is not due to bactericidal properties in the blood. There are pathological-anatomical differences between the lesions of encephalitis lethargica and poliomyelitis, and there is no cross-immunity. The clinical features of the disease in man are variable, and it is probable that there are attenuated varieties of the virus. By cultivation of the cells of the infected testicle *in vitro* it was found that the virus could survive for 15 days at 37° C. No actual cultures of the virus have, however, been obtained.

In the second paper the authors describe the effects of intramuscular, intraperitoneal, and intradermic inoculation of the virus, as well as the virulence of the spinal ganglia and the action of bile on the virus. The authors emphasize the fact that the encephalitis virus presents a close analogy to that of rabies. Like the latter, bile is destructive to the virus of lethargic encephalitis. W. B.

**Amoss, H. L.** **Immunological distinctions of encephalitis and poliomyelitis.** *J. Exper. M.*, 1921, **33**, 187.

This is a series of seven experiments in monkeys (*M. rhesus*) which were all inoculated with a passage strain of the virus of poliomyelitis which produced paralysis and death in a week. Monkeys which received normal human serum, immune poliomyelitic serum, or the serum from cases of lethargic encephalitis, intraspinous, were subsequently inoculated in the same region with virulent passage virus of poliomyelitis. With the exception of the animal that received immune poliomyelitis serum and remained well, they all died with the microscopic signs of experimental poliomyelitis. The author concludes that the two diseases are not identical and can be distinguished by the properties of the blood-serum, a view which has also been upheld by Levaditi and Harvier (*vide supra*). W. B.

**Sörensen.** Mikroskopische Untersuchungen von Influenzaorganen. [**Microscopic examination of the organs from cases of influenza.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **91**, 204.

A short but clear description of the histology of the organs of 27 cases of influenza. The author thinks that the fact that two or more different bacteria are to be found in influenza indicates that they are secondary invaders rather than the true causes of the disease. He thinks that the explosive character of influenza is more in harmony with an unknown agent—possibly ultramicroscopic. W. B.

**Branham, Sara E.,** and **Hall, Ivan C. Influenza studies. Attempts to cultivate filtrable viruses from cases of influenza and common colds.** *J. Infect. Dis.*, 1921, **28**, 143.

This describes an attempt to cultivate filtrable viruses from certain respiratory diseases, such as colds and influenza, the nasopharyngeal secretions from 44 persons having been examined. The series include eight normal people. The secretion was obtained by washing out the nasopharynx with Ringer's solution. In order to determine the efficacy of the filter a quantity of *B. prodigiosus* was added before filtration. The filtrate was tested on a variety of complicated media mostly containing serum or a substitute such as ascitic fluid with or without fresh tissue. In a number of instances *B. prodigiosus* and even other bacteria were found to have traversed the filter surface. Other technical errors were also revealed. In a number of experiments in which neither of these factors operated incubation revealed a haziness in the medium, but it was also met with in fluids obtained from normal persons, and even in uninoculated media. The results of the work were therefore negative. W. B.

**Cecil, Russell L.,** and **Steffen, G. I. Acute respiratory infection in man following inoculation with virulent *Bacillus influenzae*.** *J. Infect. Dis.*, 1921, **28**, 201.

After a review of the attempts that have been made to produce influenza in man by direct inoculation of cultures of *B. influenzae* into the healthy nose and throat, the author gives an account of his own experiments, six in number, in addition to six other inoculations which were performed with filtrates of influenza cultures, *Streptococcus haemolyticus* or pneumococcus type IV. The volunteers selected were healthy adults, either medical students or laboratory workers, and of the six inoculated with cultures of *B. influenzae,* three gave a history of influenza during the epidemic of 1918–19. The other three denied having had the disease. In each case preliminary cultures were taken from the nose and throat to eliminate influenza carriers. One carrier was, however, intentionally selected to determine whether the presence of influenza bacilli in the nose and throat conferred immunity against experimental infection. After inoculation all the inoculated were carefully observed. Case 1 received in each nostril half a slant, in 0·5 c.c. bouillon, of an 18-hour chocolate blood-agar culture of *B. influenzae.* There was slight malaise for several days and frontal headache lasting 24 hours. The injected bacilli rapidly disappeared from the nasopharynx. Case 2 received an entire sloped culture in each nostril, the culture being the third generation on artificial media. In little more than an hour he complained of headache and a burning sensation in the nose accompanied by considerable serous discharge. Later he had malaise, drowsiness, and tender glands at the angles of the jaw. Temperature and leucocytes were unaffected. Smears from the throat showed many pus cells and intracellular influenza bacilli which however could not be recovered after 24 hours. Two other volunteers (3 and 4) received doses of peritoneal exudate taken directly from a rhesus monkey that had succumbed in 24 hours to a massive dose of *B. influenzae.* Case 3 received 0·1 c.c. of peritoneal exudate from the monkey and became affected with headache, rhinitis, malaise, pharyngitis, tracheitis, and backache. The symptoms subsided, but a relapse occurred with profuse nasal discharge which was purulent and contained many influenza bacilli which were still present two weeks after inoculation. Case 4 rapidly developed the symptoms of mild influenza with marked prostration, headache, and pains in the limbs. There was also a definite leucopenia. Influenza bacilli persisted in the throat for four weeks. Case 5 received 0·5 c.c. of a young blood-broth culture recently isolated and was attacked with similar symptoms, the leucopenia being especially marked. Case 6, who prior to inoculation was known to be a carrier, passed through a mild attack as a result of the inoculation of a blood-broth culture. Two volunteers (7 and 8) who received 0·5 c.c. of the filtrate from a 6-hour-old broth culture of *B. influenzae* showed no symptoms. Cases 9 and 10 received 0·5 c.c. of a blood-broth culture of *Streptococcus haemolyticus* freshly isolated from the tonsils of a young woman suffering from acute follicular tonsillitis and peritonsillar abscess. In Case 9 no untoward effects were produced, whereas Case 10 developed an acute follicular tonsillitis which, however, lasted only a few days. There was also moderate fever and leucocytosis.

Cases 11 and 12 received 0·5 c.c. of a blood-broth culture of a highly virulent pneumococcus type IV isolated from the sputum of a child with influenzal pneumonia. In neither case did symptoms ensue. Agglutination and absorption tests were carried out by Povitsky on the strains recovered from the patients after inoculation, and in every case they proved to be identical with the strain inoculated. Cases 3 and 6 were of special interest. In the first of these, the bacilli taken from the first attack and from the relapse differed agglutinogenically. In the case of No. 6—an influenzal carrier—the strain inoculated and the strain he carried were unlike. On the third day of his illness both strains were recovered, while after a week the inoculated strain had disappeared, the carrier strain alone surviving.

W. B.

**Olitsky, P. K.,** and **Gates, F. L.** (1). **Experimental studies of the nasopharyngeal secretions from influenza patients. I. Transmission experiments with nasopharyngeal washings.** *J. Exper. M.*, 1921, **33**, 125.

**Olitsky, P. K.,** and **Gates, F. L.** (2). **Experimental studies of the nasopharyngeal secretions from influenza patients. II. Filterability and resistance to glycerol.** *J. Exper. M.*, 1921, **33**, 361.

**Olitsky, P. K.,** and **Gates, F. L.** (3). **Experimental studies of the nasopharyngeal secretions from influenza patients. III. Studies of the concurrent infections.** *J. Exper. M.*, 1921, **33**, 373.

The object of the investigation was to determine whether the secretions of the nasopharynx of individuals suffering from epidemic influenza produced any change in animals which could not be produced by similar secretions from normal persons. The inoculum employed consisted of unfiltered nasopharyngeal washings, filtered washings, pulmonic tissue suspensions, filtered and unfiltered, from previously inoculated rabbits, similar pulmonic tissue conserved in 50 per cent. glycerol, bacteria and culture materials, and control materials. Rabbits were the animals employed, and the materials were introduced into the trachea by means of an intratracheal catheter or through a tracheotomy wound. Unfiltered nasopharyngeal washings from 8 cases of influenza within the first 36 hours of the disease produced symptoms in 7 instances, whereas similar materials from 12 cases after 36 hours were negative. The symptoms observed in the rabbits were fever after an incubation period of 24 to 48 hours, ruffled hair, conjunctivitis, marked leucopenia lasting 3 days. If the rabbits were killed—none died from the infection—the lungs were exclusively affected and had a mottled haemorrhagic appearance. When incised a blood-stained frothy liquid dripped from them. Microscopically there were haemorrhagic foci, oedema, and emphysema. No ordinary bacteria could be found by microscopic examination or by culture. In some cases similar lesions were produced even when cultivable bacteria were present, although, in transmitting the experimental condition in series, the bacteria are gradually eliminated. The fact that the condition was transmitted in series led the authors to conclude that there was an infective substance which was not composed of ordinary bacteria or their products. The substance is stated to be filterable and to be capable of surviving and apparently multiplying in association with ordinary bacteria in the nasopharynx of man or in the lung of the rabbit.

In the second paper it is shown that the lesions in the lungs and circulation can also be produced by Berkefeld filtrates from the lungs of rabbits, and that the lesions can be propagated in series by filtrates. In one series filtrates were propagated successfully through seven rabbits. Guinea-pigs were also found to be affected by filtrates in the same manner as rabbits. The supposed agent was found to withstand a 50 per cent. solution of glycerol for periods up to nine months.

The third paper deals with concurrent infections and the effect of the transmissible agent upon them. The authors believe that the influenzal agent exerts an effect on the pulmonic tissue which encourages the invasion of the lung and the subsequent multiplication there of ordinary bacteria such as pneumococcus, streptococcus, and *B. influenzae.* With the 'influenzal agent' alone none of the experimental animals succumbed, whereas death was met with when certain bacteria were present in addition.

W. B.

**Park, W. H., Williams, Anna W.,** and **Krumwiede, C.** **Microbial studies on acute respiratory infection with especial consideration of immunological types.** *J. Immunol.*, 1921, **6**, 1.

I. **Williams, Anna W., Nevin, Mary, Gurley, Caroline R.,** *et aliae.* **Methods of demonstrating micro-organisms, including 'filtrable viruses' from upper respiratory tract in 'health', in 'common colds', and in 'influenza', with the object of discovering 'common strains'.** *Ibid.*, 1921, **6**, 5.

II. **Cooper, Georgia M., Mishulow, Lucy,** and **Blanc, Ninette E.** **A study of the serological relationships of pneumococci from the upper respiratory tract, with special reference to common colds and influenzal conditions.** *Ibid.*, 1921, **6**, 25.

III. **Williams, Anna W., Unneberg, Aarlang, Goldman, Agnes,** and **Hussey, Helena.** **Relationship to upper respiratory infections of streptococci producing a green zone on standard blood-agar plates (Smith and Brown's alpha type).** *Ibid.*, 1921, **6**, 53.

IV. **Povitsky, Olga R.,** and **Denny, Helen T.** **Further studies on grouping of influenza bacilli, with special reference to permanence of type in the carrier.** *Ibid.*, 1921, **6**, 65.

V. **Park, W. H.,** and **Cooper, Georgia.** **Accidental inoculation of influenza bacilli on the mucous membranes of healthy persons with development of infection in at least one. Persistence of type characteristics of the bacilli.** *Ibid.*, 1921, **6**, 81.

VI. **Coca, Arthur F.,** and **Kelley, Margaret F.** **A serological study of the bacillus of Pfeiffer.** *Ibid.*, 1921, **6**, 87.

VII. **von Sholly, Anna I.,** and **Park, W. H.** **Report on the prophylactic vaccination of 1,536 persons against acute respiratory diseases, 1919–20.** *Ibid.*, 1921, **6**, 103.

This group of papers records the results of a series of co-ordinated researches carried out in New York City. These researches form a part of an investigation on the aetiology and prevention of acute respiratory diseases being carried out in Boston, Chicago, Washington, and New York.

The special points for investigation in this group are:

(1) A study of the micro-organisms in the upper respiratory tract in health, in common colds, and in influenza.

(2) An endeavour to establish the relationship of the influenza bacillus to both pandemic and sporadic cases of influenza.

(3) A study of the permanence of type characteristics of influenza bacilli in persons after recovery from respiratory infections.

(4) A study of the incidence of common colds, influenza, and pneumonia, following the use of vaccines made up of different types of bacteria claimed to cause acute respiratory diseases.

In paper I details of the methods of collecting material for investigation are given fully, and tables show the average comparative incidence of groups of micro-organisms in health and in disease.

From aerobic cultures of unfiltered material the cultured results were greatly influenced by the area from which the material was obtained and the variety of medium used.

From anaerobic cultures of filtered washings by the Noguchi technique, from 10 consecutive cases of influenza, 4 showed a minute coccoid organism which could not be cultivated for more than one generation. No animal inoculations were attempted. Of 23 cases of early rhinitis two showed cocci which rapidly died out.

The table giving the case incidence of the groups of micro-organisms found shows that the green-producing streptococcus is present in 100 per cent. of influenza cases, and in 91 per cent. of colds, and 89 per cent. of normal persons ; *B. influenzae* is present in 92 per cent. of influenzas, 65 per cent. of colds, and 40 per cent. of normals ; haemolytic streptococci in 27 per cent. of influenzas, 16 per cent. of colds, and 6 per cent. of normals ; and the pneumococcus in 50 per cent. of influenzas, 39 per cent. of colds, and 26 per cent. of normals.

In paper II are recorded details of investigations carried out to determine whether any one variety of pneumococcus would be encountered more frequently in epidemic inflammatory conditions resembling influenza than in those of the nature of ordinary colds or in normal controls.

The methods of collecting and examining material were similar to those used throughout this series of investigations. The methods employed to determine similarity or dissimilarity of strain were those of agglutination and absorption of agglutinins. The criteria for identification of an organism as a pneumococcus were typical morphology and bile solubility.

Of 138 cases cultured, pneumococci were found in 53. Strains were obtained from 47 of these cases and were tested with the three type sera. Of the 47 strains, 9 were found to fall into fixed types by agglutination. These were : Type I, pneumococci from two normals and one influenza case ; Type II, from two influenza cases ; Type III, four strains, one each from chronic rhinitis, acute rhinitis, pharyngitis, and influenza. Of the remaining 38 strains, 15 showed some delayed or partial agglutination with group II serum. Eleven strains were slightly agglutinated by all the type sera.

Monovalent sera were prepared from 22 strains, and cross agglutination with heterologous strains was shown to be very slight.

The agglutinin absorption experiments indicate that these strains form a number of small sub-groups, and it is concluded that there is not a particular type of pneumococcus prevalent in any of the conditions studied.

It is also noted that in twenty-five cases from which several strains were isolated, all the strains from an individual case were similar with one exception.

Paper III deals with the relation of the streptococci, producing a green zone on blood-agar, to the respiratory conditions which are under consideration. This paper forms a preliminary report which the authors propose to continue at a later date. Their findings at present are that these streptococci form a group in which a multiplicity of strains exists, and, further, that no one combination predominates significantly over another in any clinical case group.

Paper IV records the results of attempts to group influenza bacilli and to demonstrate permanence of type or otherwise in carriers. The chief method used has again been agglutination and absorption of agglutinin.

100 old and 90 new strains were tested with 30 sera. Very little evidence of dominant types could be obtained even amongst cases attacked in the same locality at the same time. These general findings were in support of those of Valentine and Cooper.

Of seven strains found in cases of influenzal meningitis four were found to fall into one serological group, while the other three were not agglutinated by, nor did they absorb with any except a homologous serum.

In one group of 5 persons, a mother and four children, 10–20 colonies were isolated from each person. It was found that the colonies obtained from each member were not all identical with each other. Homologous sera were prepared against one strain isolated from each of two members of the family. These sera were tested with a number of strains from each case. It was found that each child possessed members of the mother's majority strain, but that they were not necessarily majority strains in the children.

In other cases examined it was found that repeated isolation of strains from a given case produced bacilli serologically identical on each occasion.

Similarly it was found that carriers usually continued to carry the same serological strain with which they were originally infected. In one case, however, a complete change of strain was demonstrated. On testing their series of strains for indol production the authors find that 75 per cent. of typical influenza bacilli form indol. Cultural and immunological grouping do not always coincide.

Paper V records three accidental inoculations with known cultures of *B. influenzae.* Of these three cases one developed the disease 4 days later, another developed a temperature 101° F., prostration, and general pains 14 days after infection, and the third did not develop any symptoms. All three cases became carriers, and all the strains isolated after varying periods retained their agglutination characteristics unchanged. A fourth case accidently inoculated neither had symptoms nor became a carrier.

Paper VI gives details of experiments carried out with 6 groups of cultures of *B. influenzae* to ascertain whether a definite pandemic strain could be demonstrated. Antisera were prepared against 8 different cultures and each was tested by direct agglutination against all of the cultures included in this study (18 in all). Absorption tests were also carried out with some of the sera.

The results of the experiments show that cultures isolated in different localities at different times cannot be grouped together as identical in characteristics. In the course of this work one immune serum was found to agglutinate heterologous strains while it did not agglutinate the strain used in preparing the immune serum.

Experiments carried out to investigate this phenomenon indicate that it was due to the presence of a specific inhibiting antibody.

Paper VII records the results obtained from prophylactically inoculating 1,536 persons against acute respiratory diseases.

The group of persons inoculated were drawn from the employees of the Metropolitan Life Insurance Company's Home Office, New York City. As a control group, 3,025 persons of similar age and both sexes, working at the same offices, were observed.

Of the total, 1,293 received three inoculations,

| | | | |
|---|---|---|---|
| 95 | „ | two | „ |
| 148 | „ | one | „ |

The vaccine employed and used in the larger group of 1,412 persons was made up as follows:

| | | | |
|---|---|---|---|
| *B. influenzae* | 1,000 | million | per c.c. |
| *Streptococcus haemolyticus* | 1,000 | „ | „ |
| „ *viridans* | 1,000 | „ | „ |
| Pneumococcus Type I | 2,000 | „ | „ |
| „ „ II | 2,000 | „ | „ |
| „ „ III | 2,000 | „ | „ |

A smaller group of 124 persons were given a vaccine containing:

| | | |
|---|---|---|
| Pneumococcus Type I | 10 per cent. | *āā.* 1,500 million per c.c. |
| „ „ II | 14 „ | |
| „ „ III | 6 „ | |
| Pneumococcus Group IV and allied green-producing diplostreptococci | | 1,500 „ „ |
| *Streptococcus haemolyticus* | | 1,000 „ „ |
| *Staphylococcus aureus* | | 500 „ „ |
| *B. influenzae* | | 500 „ „ |

Details are given of the various reactions recorded after the inoculations.

Tables also show the incidence of various types of respiratory infections amongst the inoculated and amongst the controls during the winter subsequent to inoculation. The figures for each group for past winters are given for comparison.

It is not easy to arrive at a conclusion owing to the fact that the uninoculated group had in previous winters been less subject to respiratory infections than the inoculated group. This selection, due to the fact that the inoculated group were volunteers, detracts from the value of the investigation. The authors conclude, however, that 'On the whole our evidence does not make a strong case in favour of the vaccines given by us as a prophylactic agent against acute respiratory diseases—pneumonia alone excepted.' G. T. W.

**Séguin, P.** Culture des spirochètes buccaux favorisée par quelques bactéries. **[The beneficial effect of certain bacteria in the cultivation of buccal spirochaetes.]** *Compt. rend. Acad. d. sc.*, 1920, **171**, 1243.

Séguin finds that certain organisms such as *Staphylococcus albus, B. fusiformis, Streptococcus viridis*, &c., greatly facilitate the growth *in vitro* of buccal spirochaetes. *S. viridis* is the best for *Sp. dentium*, which may be obtained in pure culture by using Noguchi's medium (fresh tissue serum agar). In the case of another spirochaete with flattened curves and with attenuated extremities, which Séguin terms *Sp. acuta*, he found that the presence of *B. fusiformis* is essential to its growth. *Sp. acuta* cannot be grown by itself even though an isolated colony is used for subculturing. But if a collodion capsule containing a culture of *B. fusiformis* is immersed in a tube of ascitic fluid agar inoculated with *Sp. acuta*, colonies of the latter will appear in the vicinity of the capsule. Some of the cultures have been kept alive for 18 months. J. R. P.

**Palmén, A. J.** Ett i Helsingfors observeradt fall af sodoku eller den japanska råttbettsjukdomen. [**A case of rat-bite fever in Helsingfors.**] *Finska Läk-sällsk. Handl.*, 1920, **62**, 586–98.

**Nicolaysen, N. A.** Et tilfælde af Rat-Bite Fever (Sodoku). [**A case of rat-bite fever.**] *Med. Rev.*, 1920, **37**, 164–72.

Palmén's patient was a railway porter whose left index finger was bitten by a rat. Intermittent fever, accompanied by rigors, developed, and a spotty eruption appeared over the whole of his body. He complained of malaise and headache, and there was a painful and tender gangrenous patch, measuring 2 by 2 cm., corresponding to the position of the rat-bite. The bacteriological examination of this lesion showed staphylococci and streptococci as well as rods of unequal length. Numerous leucocytes were also found. Examination of the blood showed a normal relation between the white and red blood-cells, and there was no marked increase of the eosinophil cells. With Giemsa staining numerous blood-platelets were found, as well as certain structures resembling the sporoblasts described by Ogata in connexion with sodoku. These structures may, however, simply have been formed by the clumping of blood-platelets. No spirochaetes could be found either in the blood or in blood-cultures (Löffler's blood-serum-agar, ascites-agar plates, ascites-bouillon, and indigo-ascites-agar). The results were also negative on culture of matter, taken from the primary lesion, on the same media. Complete recovery followed the intravenous injection of neosalvarsan.

In Nicolaysen's case there was no history of a rat-bite, but the patient, a woman aged 23, had played with cats and handled other domestic animals. The primary lesion occurred on the back of the proximal phalanx of the right ring finger. In spite of a persistent search for the infecting organism at Gade's Pathological Institute in Bergen, no spirochaete or other microorganisms could be found. There was no sign of syphilis, and the clinical picture, including the recurrent fever, conformed so exactly to that of sodoku that, in spite of the absence of a history of a rat-bite, injections of neosalvarsan were given. Recovery promptly followed. Nicolaysen suggests that the protozoal organism responsible for rat-bite fever leads a saprophytic existence in the mouths of animals other than the rat, and he refers to cases of typical rat-bite fever following the bites of the cat, polecat and squirrel.

C. L.

**Besson, A., et de Lavergne.** Sur le bacille de Morgan. [**On Morgan's bacillus.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 77, 530.

In a short study of Morgan's bacillus, the authors assert that it ferments, with gas production agar containing glucose, laevulose, galactose, and glycerine. Maltose may be affected late (48 hours) and the medium at first red may become blue. In agar media, lactose, mannitol, saccharose, and dulcitol are not fermented although in liquid media the last of these is attacked. One race examined is also said to have slightly fermented lactose with minimal gas production. According to the authors lead acetate is never blackened, a result at variance with that of some other authors. Indol production was abundant and rapid. The virulence for animals is variable and, in general, slight. With virulent strains subcutaneous inoculations produce slight local lesions in rabbits, guinea-pigs, and mice, whereas intravenous injections in rabbits are fatal, the bacilli being recovered from the blood, the intestinal contents, the bile, and the urine. The authors attribute this to endotoxin formation, as fatal results are obtained from cultures killed by heat or ether. With large doses (3 c.c.) the symptoms are sudden and profound collapse, dyspnoea, and convulsions, death occurring in a few minutes. In doses up to 1 c.c. there may be diarrhoea and paraplegia. The autopsy shows subcutaneous and visceral ecchymoses, great congestion of the vessels of the bowel and kidneys with sanguinolent diarrhoea.

In the second paper (p. 530) the authors make a study of the serum reactions with Morgan's bacillus and say it is not a homogeneous species. They think that the bacillus should be classed in the Salmonella group.
W. B.

**BLUMENTHAL, G.** Zur Ätiologie der bazillären Ruhr. [**On the aetiology of bacillary dysentery.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **91**, 335.

The author has studied a series of strains of dysentery bacilli isolated in Galicia in 1917. He found—as others have done—that a number cannot be placed in the classical groups by agglutinating sera, this applying particularly to Flexner-Y sera. He recommends the use of polyvalent sera made by inoculating rabbits with Kruse's races A, D, and H, and in addition a monovalent serum made from Kruse's race E. According to him Schmitz's bacillus corresponds agglutinogenically with Kruse's race J. W. B.

**BACH, F. W.** Vergleichende Untersuchungen über Proteus-Stämme unter besonderer Berücksichtigung des sogenannten Hämotoxinbildungsvermögens. [**Comparative studies on races of Proteus, with special reference to their capability to produce haemotoxin.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1921, **85** (Orig.), 305.

A long paper dealing chiefly with the haemolytic properties of cultures of *Proteus vulgaris*. All cultures of this organism are capable of laking blood corpuscles. In bouillon medium the maximal haemolytic power was attained in 5 to 6 hours, disappearing usually at the end of 24 hours. Exclusion of oxygen has no influence on the laking property. Boiling the cultures for 2 minutes usually sufficed to destroy the lysin, but not always. It is doubtful whether the lysis is due to a genuine haemotoxin as an antihaemotoxin could not be prepared. W. B.

**AOKI, K.,** u. **IIZUKA, N.** Studien über die Unterarten der Proteusbacillen. Die gekreuzte Agglutination als ein Differenzierungsverfahren der Bakterienunterarten. [**Studies on the sub-groups of *Proteus*. Cross-agglutination as a differential-diagnostic means.**] *Tohoku J. exp. Med. Sendai*, 1920, **1**, 493.

The authors have carried out an elaborated investigation on the differentiation of *Proteus vulgaris*, *P. mirabilis*, and *P. zenkeri*, especially by cross-agglutination tests. Forty-one strains of *Proteus* were isolated, chiefly from pathological lesions in man, and they were first subdivided according to Hauser's original plan, by their ability to liquefy gelatin. By this test 20 corresponded to *P. vulgaris*, 14 to *P. mirabilis*, and 7 to *P. zenkeri*. Agglutination experiments were then undertaken with the sera of immunized rabbits. By cross-agglutination experiments they showed that 20 strains of *P. vulgaris* fell into 7 sub-groups, 14 of *P. mirabilis* into 5 sub-groups, and 7 of *P. zenkeri* into 3 sub-groups. The groups differentiated by the agglutination test did not correspond to the groups by the cultural differentiation. The cultural characters were also found to be unstable, whereas the agglutinogenic differentiation was more constant and durable. W. B.

**Wishart, Mary B.**, and **Pritchett, Ida W.** **Experimental studies in diabetes. Series II. The internal pancreatic function in relation to body-mass and metabolism. 6. Gas bacillus infections in diabetic dogs.** *Am. J. Physiol.*, 1920, **54**, 382.

In the course of researches on experimental diabetes four dogs died of gas bacillus infection. As such infections are rare in these animals it was decided to make experiments to determine (1) whether susceptibility to such infections is increased by reason of the excess of circulating sugar or a specific diabetic lowering of resistance; (2) whether an aggravation of the diabetic condition is demonstrable in such infections. Three partially depancreatized diabetic dogs were inoculated intramuscularly with pure cultures of *B. welchii*. Local necrosis and gas formation were observed, but without peritoneal or systemic infection. There was no evidence of an acquired disposition either from the diabetes itself or from the excess of sugar in the blood. The latter point was emphasized by the fact that the reactions were essentially similar in the first dog with mild glycosuria, in the second with heavy glycosuria, and in the third dog, which, by suitable diet, was at the time of inoculation free from glycosuria. W. B.

## BIOCHEMISTRY

**White, H. L.**, and **Erlanger, J.** **The effect on the composition of the blood of maintaining an increased blood-volume by the intravenous injection of gum acacia in normal, asphyxiated, and shocked dogs.** *Am. J. Physiol.*, 1920, **54**, 1.

A strongly hypertonic glucose and gum acacia solution (18 per cent. glucose and 25 per cent. gum acacia) which has been found useful in the treatment of shock, was injected intravenously into normal, asphyxiated, and shocked dogs, and the resultant changes in blood-volume and composition were studied. The immediate effect was a marked increase in blood-volume; in normal and asphyxiated animals the blood-volume then gradually fell toward, but did not completely return to, normal in several hours. The blood-volume, markedly diminished in shock, is increased to above its normal level by the injection and then gradually falls to or below its normal level. The absolute plasma protein is increased slightly or not at all in normal animals and in asphyxiated animals. The absolute amount of plasma protein is markedly diminished in shock, is increased by the injection, and the increase continues for some time after the injection. It is believed that at least a part of the increase in plasma protein following the injection in shock is due to a passage of protein in through the vessel walls.

Gum acacia seems to take the place of plasma protein in holding water in the circulation.

There is a marked hyperglycaemia immediately after the injection. The blood-sugar value falls to, or nearly to, normal within two hours. The fluid drawn into the blood-stream brings with it chlorides in concentration equal to the chloride concentration of plasma, but the diffusion into the blood-stream of sufficient additional chlorides to bring the chloride concentration of injected fluid up to that of plasma is not complete for several hours. The entrance of urea into the plasma takes place with such facility that the non-protein nitrogen concentration of the plasma remains constant.

There is no suppression of urine in normal animals as a result of the injection; if anything, the rate of secretion is slightly increased.

The crystalloid osmotic tension of the plasma does not remain constant.

No haemolysis, haematuria, haemoglobinuria, albuminuria, cylindruria, fluctuations in body-temperature, or any other untoward effects, were observed as a result of the injections. W. C.

**Ross, E. L.,** and **Davis, L. H. A difference between the mechanism of hyperglycaemia production by ether and by chloroform.** *Am. J. Physiol.*, 1921, **54**, 479.

A group of dogs was anaesthetized with ether for half an hour. The next day the dogs were anaesthetized with the same drug for fifteen minutes. The blood-sugar changes were measured for the first fifteen minutes of anaesthesia both times. A second group of dogs was anaesthetized with chloroform for half an hour, and the following day each was given fifteen minutes of ether anaesthesia. The blood-sugar changes the second day were measured. A third group of animals fasted two days and was then treated the same as the second group.

Half an hour of ether anaesthesia did not alter the blood-sugar percentage of the following day, and did not decrease the hyperglycaemia resulting from fifteen minutes of ether anaesthesia. Half an hour of chloroform anaesthesia produced on the following day a blood-sugar lower than normal, and an increase in blood-sugar due to fifteen minutes of ether anaesthesia less than normal. A fast of two days preceding half an hour of chloroform anaesthesia produced on the following day a still lower blood-sugar and still less reaction to fifteen minutes of ether anaesthesia than occurred in non-fasting dogs.

These results, in conjunction with the conclusions of Davis and Whipple that the liver injury produced by chloroform is increased by a fast preceding anaesthesia, lead to the following conclusions:

1. Ether anaesthesia does not produce any injury to the mechanism of dextrose mobilization that can be detected the following day.
2. The injury to the liver-cells produced by chloroform anaesthesia reduces the blood-sugar of the following day, and injures the mechanism of dextrose mobilization according to the degree of injury.
3. The hyperglycaemia due to chloroform anaesthesia is not due primarily to the direct action of chloroform on the liver. Probably chloroform, like ether, produces hyperglycaemia chiefly through its depressing action on the internal secretion of the pancreas. W. C.

**Marine, D.,** and **Lenhart, C. H. The influence of glands with internal secretions in the respiratory exchange. I. Effect of subcutaneous injection of adrenalin on normal and thyroidectomized rabbits.** *Am. J. Physiol.*, 1920, **54**, 248.

A number of workers have shown that the injection of adrenalin causes an increase in the gaseous metabolism in man. The authors' observations on rabbits confirm this result for both normal and thyroidectomized rabbits. As the result of thyroidectomy the metabolism falls in rabbits as it does in other animals. This decrease is gradual and requires several days for its demonstration. The main difference in the reaction of thyroidectomized rabbits to the injection of adrenalin is that the onset of the rise in oxygen consumption is delayed and does not last as long as in normal animals. W. C.

**Aub, J. C., Cunningham, T. D.,** and **Wu, H. Studies in experimental traumatic shock. I. The basal metabolism. II. The oxygen content of the blood. III. Chemical changes in the blood.** *Am. J. Physiol.*, 1920, **54**, 388.

The gaseous metabolism was studied in cats under urethane anaesthesia. Experimental shock produced by crushing the hind legs caused a marked fall in the rate of basal metabolism to 70 per cent. of the original level. A similar fall may be produced rapidly by interference with the circulation by increased pericardial pressure. The effect of haemorrhage is not constant: it may lower the basal metabolism or have no immediate effect. Recovery from shock after blood transfusion is usually associated with a prompt return of the basal metabolism to the normal level.

The oxygen content of blood is greatly diminished in experimental traumatic shock. This change precedes the fall of the blood-pressure and is still present after apparent recovery from shock. The blood-flow is also greatly decreased. The resultant anoxaemia of the tissues is probably the cause of the great fall in metabolism.

Chemical examination of the blood showed a great increase in the creatin and in the blood-sugar in shock. The non-protein nitrogen and urea also rise, but not to the same extent. The rise in creatin is direct evidence of the presence in the blood of products of muscle necrosis and is looked upon as suggestive evidence for the theory of the chemical cause of traumatic shock. The rise in the blood-sugar, which is discussed, is not clear. W. C.

**Allen, F. M. Experimental studies in diabetes. Series II. The internal pancreatic function in relation to body-mass and metabolism. 5. The influence of fever and intoxication.** *Am. J. Physiol.*, 1920, **54**, 375.

**Wishart, M. B.,** and **Pritchett, T. W. Experimental studies in diabetes. Series II. The internal pancreatic function in relation to body-mass and metabolism. 6. Gas bacillus infections in diabetic dogs.** *Am. J. Physiol.*, 1920, **54**, 382.

Infections are known to be among the most effective agencies in aggravating human diabetes. The first paper is a record of observations on the effect of chance infection in partially depancreatized dogs. The observations show a great difference between clinical and experimental diabetes. For in dogs even severe infections, such as peritoneal abscesses, general peritonitis, pneumonia, do not aggravate the diabetes. The author suggests, however, that the difference may be one of degree rather than of kind, because, as shown in the second paper, a lowering of tolerance could be demonstrated when infection was produced experimentally with cultures of *B. welchii.*

The author believes that the aggravation of human diabetes is a reaction to intoxication rather than to fever, and that no specific aggravation of diabetes or lowering of tolerance results from the metabolic alteration attendant upon elevation of body temperature in experimental animals.

W. C.

**Allen, F. M. Experimental studies in diabetes. Series II. The internal pancreatic function in relation to body-mass and metabolism. 7. The influence of cold.** *Am. J. Physiol.*, 1921, **54**, 425.

Cold is stated to produce hyperglycaemia and glycosuria in normal animals and to increase the glycosuria of normal dogs. In this paper the effect of cold was studied in partially depancreatized dogs. It was found that as a rule cold environment, such as did not lower the rectal temperature, produced in most cases hyperglycaemia and sometimes glycosuria. These were produced more easily and in higher degree in proportion as the power of utilization of sugar was impaired, i. e. as the diabetes was more severe.

The author strongly insists that cold itself is not diabetogenic, and that one must make a clear distinction between the power to produce glycosuria and the power to produce diabetes. The former is due to a mobilization of carbohydrate, the latter to an impairment of the utilization of sugar. Experimentally the influence of cold is not equivalent to the removal of the smallest fraction of a gramme of pancreatic tissue, and there is no demonstrable difference in the proportion of pancreatic tissue that must be removed to produce diabetes in dogs in warm or cold environment.

The impression that diabetic patients do worse in cold weather is probably explainable by the discomfort of chilliness when they are undernourished, the tendency to take more food, and sometimes by the limitation of exercise. These may be important sometimes from a practical standpoint, but any direct influence of climate upon diabetes must be slight, if it exists. W. C.

**Allen, F. M. Experimental studies in diabetes. Series II. The internal pancreatic function in relation to body-mass and metabolism. 8. The influence of extremes of age upon the production of diabetes.** *Am. J. Physiol.*, 1921, **54**, 439.

Observations on senile dogs failed to show any departures from the normal in the glucose tolerance, ratio of pancreas weight to body weight, microscopic appearance of the pancreas, the size of the pancreatic remnant with which diabetes occurs, the capacity of such a remnant for hypertrophy, or the clinical course of the diabetes.

In puppies the glucose tolerance is less than that of adult dogs. In regard to the other factors enumerated above, there is no striking departure from the normal, except that the capacity of the pancreatic remnant for hypertrophy is as a rule greater than in adult dogs. For this reason, and partly also on account of the greater weakness and cachexia, the tendency to diabetes is distinctly less in puppies that in normal adult dogs.

An interesting experiment is recorded in which in a puppy aged 7 months the bulk of the pancreas (8/9) was removed. A mild diabetes developed at once: on a diet containing carbohydrate glycosuria was present, which could be checked by fasting and kept absent on a suitable diet. The animal was kept alive for two years in apparent good condition. During that time the sugar tolerance diminished and hyperglycaemia was present even when fasting. Eventually after two years there was intense glycosuria with acidosis and the animal was killed. The experiment showed that a partial pancreatectomy, which barely sufficed to produce an immediate mild diabetes in a young dog, resulted in a severe diabetes after the body had grown so that the damaged pancreas had become inadequate for the demands of the bigger body-mass. From this it is easily comprehensible that diabetic symptoms may follow either soon or late after an injury of the human pancreas. Thus glycosuria may be present immediately after an infection or may be delayed to a time when there is no plain clinical connexion with a long antecedent infection which may have been the real cause. W. C.

**Suitsu, N. Studies on the alkaline reserve of the blood of the insane.** *Am. J. Physiol.*, 1920, **54**, 147.

The special object of these observations was to determine whether the carbon-dioxide combining capacity of the blood of insane patients differed from the normal, and further whether the states of depression and excitement amongst the insane exhibited any differences in the alkaline reserve.

No significant differences were observed. W. C.

**Mattill, P. M., Mayer, K.,** and **Sauer, L. W. The influence of intravenous injections of acacia-glucose solutions on urine excretion and blood-volume in rabbits.** *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 391.

Gum acacia is capable of maintaining the blood-volume in spite of marked glucose diuresis. Glucose injections without acacia produce uniformly a diminution of the blood-volume. H. E. K.

**Feucht, B.** Zur Bürkerschen Methodik der Blutkörperchenzählung. [**Bürker's method for blood-counts.**] *Arch. f. d. ges. Physiol.*, 1921, **187**, 139.

The Bürker method is stated to have every advantage over the Thoma procedure—elimination of filling error, saving of time, greater ease of manipulation, &c. The probable error is also stated to be 50 per cent. less than the smallest probable error for the Thoma instrument. A count of 80 squares is adequate except in profound anaemias. C. L. E.

**Nonnenbruch.** Über die Veränderungen im Blut nach Harnstoffgaben. [**The blood after administration of urea.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **89**, 200.

This article is a contribution to the discussion of the behaviour of urea in the body after oral administration, and, as the compound is being largely used as a test for renal efficiency, is of interest. In normal subjects the rest nitrogen in the blood was high after urea administration at a time when the excess of nitrogen had been excreted. In this case, therefore, high rest nitrogen was not an index of nitrogen retention.

By injecting urea dissolved in normal saline solution in a case of nephritis with cardiac insufficiency and oedema, the rest nitrogen in the blood only increased moderately and soon reached the previous level. The red cells decreased. Water was taken from the tissues into the blood-stream. None of the chemical indices can be used to determine whether water is being taken from the tissues to the blood or vice versa. Examination of the red cell count alone gives information on the point. C. G. L. W.

**Tredelenburg, P., u. Groebel, W.** Tetanie nach Entfernung der Epithelkörperchen und Calciummangel im Blute. [**The relation between parathyroid tetany and calcium deficit in the blood.**] *Arch. f. expcr. Path. u. Pharmakol.*, 1921, **89**, 171.

The authors have attempted to settle the much-disputed point as to whether there is a calcium deficit in parathyroid tetany. A review is given of the important literature of the various theories which have been advanced as to the causation of the condition.

They investigated the effect of the blood on the frog's heart, which is a very sensitive test object for variation in calcium content of the fluids which perfuse it. Both serum and the ash therefrom behave as if they were lower in calcium content than normal serum. Addition of a solution of calcium salt restores the properties of the tetanic product. They believe that the calcium deficit in the serum is sufficient to account for the tetany.

C. G. L. W.

**Kestner, O.** Klimatologische Studien, I. Der wirksame Anteil des Höhenklimas. [**Climatological Studies, I. The active factor in high altitudes.**] *Ztschr. f. Biol.*, 1921, **73**, 1.

Dogs were made anaemic by venesection or by the administration of pyrodin. They were then placed in a pneumatic chamber, which could be exhausted corresponding to a height of 2,500 metres. They were also exposed to the direct rays of a powerful arc lamp.

In no case did blood regeneration take place with decreased pressure alone. There was a distinct effect by irradiation: when the air from the irradiated chamber was led into another room, which was not exposed to the rays of the lamp, a similar effect was produced. Kestner believes that certain substances are formed by the action of rays which produce the well-known effects at high altitudes. This is confirmed by the experience that a stay in the mountains is beneficial even when the sky is overcast.

C. G. L. W.

**Kestner, O.** Klimatologische Studien, II. Die Wirkung der Strahlung auf den Blutdruck. [**The action of irradiation on blood-pressure.**] *Ztschr. f. Biol.*, 1921, **73**, 7.

Irradiation produces a fall in blood-pressure. This is not due to the rays themselves but to some chemical compound produced in the air. The same effect is produced on a close day followed by a thunderstorm. Attention is directed to the possible presence of nitroxyl compounds in the air.

C. G. L. W.

**Hooker, D. R. The functional activity of the capillaries and veins.** *Am. J. Physiol.*, 1920, **54**, 30.

A simple method is described whereby the peripheral circulation, particularly the capillaries and venules in the cat's ear, may be observed and photographed. Making use of this method it was found that after death by ether the peripheral vascular bed passes through a number of active changes, which depend upon a local or peripheral function, since they are not affected by nerve section and since they do not occur if an endothelial poison (histamin) has been injected. The first active change is a constriction of the capillaries which is attributed to asphyxia. This soon gives way to a marked dilatation, which is followed by a second and permanent constriction and coincident with and probably due to rigor mortis.

Section of the cervical sympathetic did not alter the calibre of the ear vessels, but electrical stimulation of the sympathetic or injection of adrenalin produced a distinct constriction. The important conclusion is drawn that the active functional peripheral resistance is not to be found wholly in the smaller arterioles with smooth muscle in their coats, but that the capillaries and venules must be included. It is inferred that this resistance is subject to chemical as well as to nervous control. This property of the capillaries represents an efficient physical mechanism for the distribution and regulation of the blood-volume and of the supply of nutriment.

The injection of histamin causes a prompt and permanent dilatation of both capillaries and venules, with stagnation of the corpuscular stream. This effect is due to a direct action of the substance on the vessels and is not influenced by nerve section. Dale's hypothesis that histamin 'shock', and presumably traumatic 'shock', is dependent upon the reaction of the capillaries is confirmed.

It is interesting to note that the observations of the author confirm, as he himself points out, some of the old observations of Lister, published in 1858, which represent the first evidence that capillaries have the power independently to change their calibre. W. C.

**Fontaine, J.** Die arterielle Blutdruckmessung beim Pferde. [**Measurement of the arterial blood-pressure in horses.**] *Arch. f. Physiol.*, 1919, 217.

Measurements of blood-pressure on horses by the Riva-Rocci apparatus. The cuff was applied to the tail artery. The blood-pressure in different horses under equal conditions of rest shows considerable individual variations. But the values found are much lower than those obtained by direct measurement with a cannula in the artery.

The blood-pressure is lower in young animals and rises with increasing age. Exercise and excitement produce a marked rise in blood-pressure. The intake of food produces a temporary fall. W. C.

**Kowallek, A.** Plethysmographische Untersuchungen über die Wirkung der Hochfrequenzströme. [**Plethysmographic investigations on the effects of high-frequency currents.**] *Arch. f. Physiol.*, 1919, 263.

High-frequency currents of measured energy in varying amounts were applied to definite parts of the body in the human subject. By plethysmographic observations and measurements of the cutaneous temperature it was then determined whether the resultant hyperaemia was only local, or whether there was a general effect.

The results show that when small amounts of energy are applied there is a local hyperaemia and the cutaneous temperature rises. If the energy is applied to the upper arm, the arm below the elbow on the same side also shows hyperaemia, but not the arm on the opposite side.

The results are discussed in detail. W. C.

**Burridge, W. Researches on the perfused heart.** *Quart. J. Exper. Physiol.*, 1920, **12**, 339.

If the frog's heart is perfused with a solution containing 0·6 per cent. NaCl, 0·03 per cent. KCl, 0·01 per cent. $NaHCO_3$, and 0·025 per cent. $CaCl_2$ for 20 to 30 minutes, and the calcium concentration is then changed to 0·01 per cent. $CaCl_2$, a very sensitive preparation is obtained, beating at about half its maximum amplitude. Such a preparation will show a marked reaction to concentrations of alcohol which have been stated by other observers to be without action. The use of hearts in different conditions of activity is a source of confusion in physiological literature. A heart beating at its maximum amplitude is not adapted to show changes produced by minimal concentrations of drugs. O. L. V. de W.

**Briggs, H. Physical exertion, fitness, and breathing.** *J. Physiol.*, 1920, **54**, 292.

Experiments carried out in the course of work on mine rescue apparatus. Physical work is easier to unfit men when air enriched with oxygen is breathed than when breathing normal air, but no such difference is observed in the fit. With work of increasing magnitude the expired $CO_2$ percentage first rises and then falls. The load at which the percentage is at its maximum is called the 'crest load', and demarcates normal loads from overloads. If curves be drawn showing work done (abscissae), and $CO_2$ percentages (ordinates), it is found that in the fit the curves on oxygen enriched and normal air closely correspond to the crest load. On the unfit, the $CO_2$ percentage is much lower with ordinary air than with enriched air, and the curves diverge. A method of measuring physical fitness is suggested, based on the degree of divergence of the curves. On an overload even the fittest men derive benefit from breathing enriched air. The benefit of breathing enriched air during the performance of physical work is limited to air containing 60 per cent. of oxygen even in very unfit persons. O. L. V. de W.

**Hewitt, J. A. The effect of the administration of small amounts of thyroid gland on the size and weight of certain organs in the male white rat.** *Quart. J. Exper. Physiol.*, 1920, **12**, 347.

Fresh thyroid in daily doses of 0·1 grm. was administered to adult and growing rats. Hypertrophy of the heart, spleen, kidneys, and suprarenals, and possibly of the pituitary, resulted. The thyroid showed a definite diminution in weight. The organs tend to resume normal proportions after resumption of an ordinary diet. O. L. V. de W.

**Haggard, H. W. The anaesthetic and convulsant effects of gasoline vapour.** *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 401.

Gasoline vapour has an anaesthetic effect somewhat like that of ethyl ether, but there is a marked convulsant action in addition. H. E. R.

**Hirsch, E. F. Rigor mortis in smooth muscle and a chemical analysis of fibromyoma tissue.** *J. Biol. Chem.*, 1921, **45**, 297.

It is an accepted view in many quarters that contraction in a muscle is the result of the change in reaction produced by the appearance of lactic acid in the muscle. This is further extended to the idea that the change of reaction induces a shortening of the muscle-fibre, after the fashion of the shortening of a catgut-string in acid. This is supported by many facts such as the appearance of lactic acid during normal contraction of a muscle and during rigor mortis. Up to date these results have been mostly obtained upon striated skeletal muscle. The author has made a contribution by studying smooth muscle (uterus) and fibromyoma, both of which contract upon going into rigor mortis, with the development of a more acid reaction. In these respects the smooth muscle resembles the striated one.

R. A. P.

**Hofmann, F. B.** Zur Theorie des Geruchssinns. I. Parosmie-Studien. [**The theory of smell. I. Parosmia.**] *Ztschr. f. Biol.*, 1921, **73**, 29.

This article gives a very interesting set of observations made by the author on himself during recovery from a severe nasal catarrh, from which he suffered a temporary complete loss of smell.

A number of compounds were taken during the period of recovery in different concentrations. It was found that these substances possessed different smells according to the time at which they were tested. Certain groups behaved differently from others, and were later in producing the characteristic smell. Hofmann believes that smell is produced by different groups of receptors of different specific energy. By the proper combination of the groups the individual has the correct perception of a characteristic smell. A very full discussion of the theoretical side of the problem is included in the paper. C. G. L. W.

**Allen, F. M. Experimental studies in diabetes. Series II. The internal pancreatic function in relation to body-mass and metabolism. 9. The influence of pregnancy upon experimental diabetes.** *Am. J. Physiol.*, 1921, **54**, 451.

No positive influence of the sex glands upon diabetes was demonstrable by extirpation experiments. Also no anatomic changes in the pancreas were perceptible with pregnancy or lactation.

Observations upon a partially depancreatized dog during pregnancy are opposed to the view that any appreciable quantity of internal pancreatic secretion passes from the foetus to the mother.

A distinct lowering of carbohydrate assimilation was shown during pregnancy. This was not clearly associated with the increase of metabolism, in the sense either of increased food requirement or new tissue formation, for it seemed approximately the same in early and late pregnancy, and was also evident during the illness following abortion. It may therefore be regarded chiefly as a toxic manifestation and thus classifiable with the influence of infection. The effect is relatively slight, because pregnancy failed to produce diabetes in a dog where the removal of 0·1 gramme pancreatic tissue sufficed for the purpose, and also, after the dog was demonstrably diabetic on carbohydrate diet, pregnancy gave rise to neither glycosuria nor hyperglycaemia on carbohydrate-free diet.

The tests with partial pancreatectomy afford the most exact method of study of the influence of pregnancy upon the internal pancreatic function by the freedom from the variables which enter into clinical cases. The slight tendency to aggravation of the diabetes and the ready control by diet support Joslin's experience of the feasibility of completion of pregnancy by diabetic women under suitable conditions of treatment. If the toxic factor is the principal one, as suggested, the possibility remains that the injurious action in some women may be considerably greater than in dogs and accordingly may require more radical measures. W. C.

**Holmes, A. D., and Deuel, jun., H. J. Digestibility of some hydrogenated oils.** *Am. J. Physiol.*, 1921, **54**, 479.

The digestibility of a number of hydrogenated vegetable oils of different origin (cotton-seed, pea-nut, and corn) and different melting-points was tested on man. The results show that these hydrogenated oils are as well utilized as natural fats of corresponding melting-points. The digestibility diminishes as the melting-point increases. The decrease is particularly marked with fats with a melting-point above 46°. W. C.

**Storm van Leeuwen, W., and Zeijdner, J. On the influence of colloids on the action of non-colloidal drugs.** *J. Pharmacol. & Exper. Therap.*, 1921, **17**, 121.

The question of relative sensitiveness to a drug may depend on the destruction of the compound *in vivo* or its combination with other substances which inactivate it. A notable instance is the resistance of the rabbit to atropin. It has been thought that this was due to the destruction of the alkaloid. The authors show that atropin is merely bound in the serum and can be released by peptone or sodium citrate, and by precipitating the serum with alcohol. Colloidal adsorption only accounts for one phase of the inactivation. C. G. L. W.

**Hansen, O. S. Magnesium sulphate in arsenic poisoning.** *J. Pharmacol. & Exper. Therap.*, 1921, **17**, 105.

It has been suggested that magnesium sulphate might be employed as an antidote in the poisoning by arsenic in salvarsan treatment. In experimental poisoning of rabbits with arsenic, life was prolonged by moderate doses of magnesium sulphate, but the salt had no effect on the fatal issue. The salt is so toxic that it cannot usefully be employed in cases of arsenic poisoning. C. G. L. W.

**Rosenmann, M.** Über Fibrinolyse. [**On fibrinolysis.**] *Biochem. Ztschr.*, 1920, **112**, 98.

A study of the conditions determining the solution of fibrin has been made. The idea is to obtain some data for application to pathological conditions such as pneumonia. A fibrinolytic substance can be extracted by alcohol from a fibrin autolysate. This substance is not identical with the tryptic ferment previously obtained by other authors from leucocytes. In the exudate of tuberculous serositis there is present a substance which inhibits fibrinolysis. Fibrin solution takes place even quicker than has been hitherto thought. A study of the effects of some salts was also made.
R. A. P.

**Weiss, M.** Die Farbstoffanalyse des Harnes. II. Das Urochromogen. [**The analysis of the colouring substances of the urine. Urochromogen.**] *Biochem. Ztschr.*, 1920, **112**, 61.

By the use of his method the author has made a study of the urochrome fraction in the urine. The substance is an acid, capable of forming salts.

It is apparently a derivative of phenyl alanine (a substance closely allied to tyrosin). With oxidation it goes through the stage of urochrome to uromelanin. The author discusses the source and biochemical meaning of urochrome in the urine. He considers that the substance has an endogenous source, and lays emphasis upon the relation to tyrosin on the one hand and melanin formation upon the other, a remarkable similarity to the alcaptonuria question. Other experiments point to the source as being ultimately nuclear. The urochrome reaction is given only by the kidney in the body, and it is natural to conclude that the urochrome is a specific secretion of the kidney formed from broken down nuclear products. The instance of hippuric acid synthesis by the kidney from glycin and benzoic acid is given in support of the fact that the kidney may play a part in the metabolism of aromatic substances. The kidney forms urochrome in a similar way to the formation of bilirubin by the liver cell. It is further interesting to note that the suprarenal has a function in pigment activities. R. A. P.

**Sullivan, M., and Dawson, P. R. Sulphocyanate content of the saliva and urine in pellagra.** *J. Biol. Chem.*, 1921, **45**, 473.

Sulphocyanate, reckoned as the potassium salt KSCN, is a normal constituent of the saliva and urine. In general it seems to arise as a synthetic product by which the body converts substances of a cyanide nature (or which give cyanide in the body) into a non-toxic substance. There seems to be some difference of opinion as to the origin of the substance in normal urine and faeces, as to how far it is endogenous or exogenous. As a result of some previous work upon the saliva of patients with pellagra, it was found by the authors of this paper that the sulphocyanate reaction (with ferric chloride and HCl) was less marked for the saliva of pellagrous patients than the normal. Upon a controlled diet they have found further that 15 out of 18 cases showed a higher content of sulphocyanate at discharge than upon entry for treatment.

Taking the urine, 11 cases out of 14 showed a higher content of sulphocyanate in the urine at discharge than at entry. This increase of sulphocyanate did not parallel the total nitrogen, so that it was not apparently a question of increased metabolism. It is hard to see exactly what these results mean, but the authors suggest that they are an index of the increased power which the body possesses of performing protective syntheses.

R. A. P.

## RADIOLOGY

### *Radium Therapy.*

**Burrows, A. Report of the Manchester and District Radium Institute, 1920.**

During the period covered by this report 834 cases came to the Manchester and District Radium Institute with a view to treatment. Of 552 cases of malignant disease 65 were rendered free from signs and symptoms of the disease during the period in question; this number does not include cases of rodent ulcer. Of these latter, 100 were treated, resulting in 45 apparent cures. The report contains the abstract of two papers, one by Shaw and Burrows on 'Wertheim's Hysterectomy for Advanced Carcinoma of the Cervix made possible by the use of Radium' and the other by Burrows and Woodburn-Morison on 'The Treatment of Exophthalmic Goitre by Radiations'. These papers were both read before Sections of the Royal Society of Medicine and will well repay close perusal. According to reports which have been issued from other centres, notably from New York, Stockholm, and Geneva, there is little room for doubt that radium treatment is proving of more and more value in cases of carcinoma of the cervix. Dr. Burrows's figures speak for themselves and his opinions become of increased value when they are established upon the results of cases of some years' standing. The technical features of this form of therapy are still to some extent matters of opinion. Dr. Burrows favours the use of large doses of radiation and the actual burying of the tubes in the cervix and the surrounding tissues; he is, however, open to other modes of administration, as, for example, a single central tube placed in the cervical canal; but this does not permit of such uniform distribution of the radiation as one obtains with five or six small tubes embedded into the growth. The dose recommended is a quantity not less than 120 mgm. of radium element operating for not less than 24 hours; if larger quantities be used the time must be correspondingly shortened. During the past year 125 cases of this disease received radium treatment, of which 32 were free from signs and symptoms at the time the report was made.

Reference is given in the report to some blood observations upon radium workers by Loveday; interesting as these are, their value would be much increased if they were more extensive; observations by Mottram have shown that profound changes occur in the blood of people subjected to frequently repeated small doses of gamma rays, and the best way to reassure the personnel of institutions where this is a possibility is to have systematic blood-tests done. There is little doubt that considerable apprehension exists at present in X-ray and radium centres as to the safeguards to health which have served in the past. If they are inadequate—and it is a matter for very close study to ensure that stray radiation is not reaching the operator—then other standards will no doubt be set up. In a growing subject like radiology stages must inevitably be reached when the general technical methods require revision and extension, but we have complete confidence that radiologists will solve a problem so essential to their good name.

The report closes with statistical tables of the various diseases treated and the general results obtained. We hope that in some later report Dr. Burrows will give data pertaining to cases of long standing as well as to those who have been under treatment during the year covered by his report. S. R.

**Tuffier.** Cancer de l'œsophage traité par l'application directe par voie transpleurale d'un tube d'émanation de radium sur la paroi œsophagienne. [**Cancer of the oesophagus treated by direct application of a tube of radium emanation to the oesophageal wall through the transpleural channel.**] *Soc. d. Chir. d. Par.*, 1919, June. (*Arch. d'électric. méd.*, 1920, **28**, 351.)

In a case of a neoplasm of the oesophagus at the level of the fifth dorsal, with neighbouring inflammatory oedema hindering any application of radium by the usual channels, the author had resort to the transpleural channel. Operative cure took place without incident, and it was evident that further treatment should be given in the natural way. S. U. L.-B.

**Guisez, J.** Traitement du cancer de l'œsophage et du larynx par des applications locales de radium. [**Treatment of cancer of the oesophagus and of the larynx by local applications of radium.**] *Paris méd.*, 1920, May. (*Arch. d'électric. méd.*, 1920, **28**, 351.)

For the introduction of the radium-carrying sound, complete stenosis of the oesophagus must not have taken place. Tubes of radium containing from 4 to 10 cgm. in a silver sheath of $\frac{4}{10}$ mm. are attached to a copper wire and fixed into a olivary sound, No. 20 or 22. The sound is first introduced into the oesophagus under endoscopy, and afterwards is controlled only by the finger. Abundant saliva is emitted by the patient, but the sound is, generally, well tolerated. Séances should take place every 7 or 8 days and the total number of applications should be at least 30. Of 61 cases improvement has been clearly effected in more than two-thirds, especially with strong doses of bromide of radium. Increase of calibre of the region of stenosis was constant. In fungating or very ulcerated forms, the action is more uncertain.

In five cases of partial extirpation of the larynx the author placed a rubber drain, size 20 to 22, containing a tube of 5 cgm. radium, in contact with the region operated upon, removing it through the thyrotomy wound. Two of the cases were too recent to enable him to judge of the results; one had a recurrence, and the other two have not recurred during the five years since treatment.

In most non-operative cases of intralaryngeal cancer the author advises tracheotomy preliminary to the application of the radium, since irradiation brings about inflammatory reactions which may cause obstruction or asphyxiation. A rubber drainage tube containing the tube of radium is introduced through the tracheal wound and is removed through the mouth. The séance should last from twelve to fifteen hours, and after three or four weeks it can be judged whether a further séance is necessary.

If the cancer is seated on the epiglottis, it is sufficient to introduce into the larynx a Botey tube, carrying transversally the radium tube on its upper part. S. U. L.-B.

**Cohen, M.**, and **Levin, I.** **The action of radium in cataract.** *J. Am. M. Ass.*, 1919, **73**, Oct. 16. (*Arch. d'électric. méd.*, 1920, **28**, 367.)

Radium has been shown to have an effect in cases of cataract by modifying the epithelium of the capsule. The technique consists in only using the most penetrating or gamma rays after cutting off all others by filtration. To effect this, the tube containing the radium salt is covered with copper, photographic paper, and gauze; the patient shuts his eyes and the tube is placed for two hours at 2 cm. from the affected eye.

In twenty patients with senile cataract treated by this method, twelve were benefited by an increase in vision without disappearance of the opacity, with a decrease in the opacity while vision remained the same, or by a complete disappearance of the opacity while the vision remained the same. P. L.-B.

**Nogier, T.** La radiumthérapie des fibro-myomes utérins. [**Radium therapy for uterine fibroids.**] *J. de radiol. et d'électrol.*, 1920, **4**, 537.

The author traces the various stages through which the treatment of fibroids has gone during the last forty years. He dwells on the great advance made by the introduction of radiotherapy, points out its disadvantages and the precautions that must be taken in its use.

In reference to radium therapy, a description is given of the technique, after-treatment, and mode of action; this is followed by a record of results obtained in a large series of cases, and the indications or contra-indications to treatment by radium. Many points in favour of treatment by radium instead of by radiotherapy or surgery are put forward.

In conclusion, the author states that the day will come when treatment by radium will be so well known that patients will come for treatment by this method earlier than used to be the case when there was the fear of an operation, and that therefore the very large fibroid or one that has undergone a malignant change will gradually be eliminated. P. L.-B.

**Béclère, A.** La radiothérapie des sarcomes de l'utérus à la clinique gynécologique d'Erlangen. [**The radium treatment of sarcomata of the uterus at the gynaecological clinic at Erlangen.**] *J. de radiol. et d'électrol.*, 1920, **4**, 529.

The paper is a critical review of a recent book written by Seitz and Wintz. They assert that in doubtful cases radium treatment will afford a better differential diagnosis between a myoma and a sarcoma of the uterus than will the microscope, since after treatment a sarcoma will show a distinct diminution in size in about a week, whereas a myoma does not begin to react for about four or five months. The writer, after indicating the technique, strongly disagrees with this assertion: he considers there is an error in the conclusions drawn, and that the reason of the slow reaction in the one case was that it was a reaction secondary to a destruction of the ovarian activity, whereas in the second case the tumour itself was directly irradiated.

The writer goes on to say that the results of the experiments confirm his own teaching, namely, that the treatment of fibromyomata of the uterus should be by direct irradiation as a whole, and that the tumour may occasionally be destroyed without destroying the organ or its function. He absolutely agrees that radiotherapy is the treatment above any other for all cases of sarcoma of the uterus, and that fear of the coexistence of a sarcoma or the possibility of a sarcomatous degeneration, cannot be brought forward as a contra-indication to the treatment of fibromyomata of the uterus by X-rays. P. L.-B.

### *Radio-diagnosis*

**Ribadeau-Dumas, Mallet,** et **de Laulerie.** L'exploration radiologique des reins, après l'insufflation intrapéritonéale. [**Radiological examination of the kidneys after intraperitoneal insufflation.**] *Paris méd.*, 1920, June, 481. (*J. de radiol. et d'électrol.*, 1921, **5**, 89.)

After reviewing the methods of radiological examination of the kidneys, the authors state their method and illustrate it by a number of examples. Intraperitoneal insufflation of about 1·5 to 2 litres of oxygen—absolutely without danger—renders the kidneys easily visible for radioscopic examination also. Radioscopic examination is made in the left lateral prone position to see the external border of the right kidney, and in the right lateral prone position to see the external border of the left kidney, and lastly in the prone position to see both kidneys.

The lower pole is clearly visible, the upper pole less so. It is easy to trace the outlines of the kidneys, and to make an orthodiagram as easily as for the heart. One can see without difficulty the presence and exact position of a calculus and to make out the size and shape of the kidneys. In the dorsal position the outline of the kidney presents an elliptical figure with the long axis slightly oblique outwards. The axis measures 8–12 cm. in a normal kidney. In nephritis irregularities are often seen on the surface of the organ, due to cortical cysts. Hydronephrosis produces an increased shadow with smooth and regular outline. Tumours of the kidney produce enlarged but irregular shadows. In polycystic disease of the kidney the large shadow shows inequalities of outline as segments of a sphere. P. L.-B.

**Forestier, J.**, et **Michon, L.** La pyélographie dans le diagnostic des kystes hydatiques du rein. [**Pyelography in the diagnosis of hydatid cysts of the kidney.**] *Paris méd.*, 1920, Oct. 16. (*J. de radiol. et d'électrol.*, 1921, **5**, 89.)

Diagnosis of hydatid cyst of the kidney presents a real difficulty and can at certain stages of its evolution be aided by instrumental methods of examination of the urinary system, particularly by pyelography. Information can be obtained by physical examination (study of the cystic tumour) and by the study of the functional signs, which are of two kinds—hydatiduria and painful phenomena. The cystoscope also should be used: it affords a complete examination of the bladder and aids diagnosis. Pyelography alone brings the greatest accuracy in diagnosis: the important information it furnishes has led Prof. Legueu to perform a conservative operation on a patient, from which she recovered with great ease.

The principles which lead to good pyelography are the following: above all things to make the injection at atmospheric pressure; never to use a syringe; to use a ureteral sound of small size; to use an opaque sound. Collargol 10–20 per cent. or sodium bromide 30 per cent. can be injected. The latter solution is not irritating, does not stain the patients, and penetrates into the tissues to a less degree than does collargol. P. L.-B.

## *Radiotherapy*

**Rocci.** X-thérapie avec nouvel appareil à 200,000 volts. [**X-ray therapy with a new apparatus giving 200,000 volts.**] *Soc. méd.-chir. de Boulogne*, 1920, May. (*Arch. d'électric. méd.*, 1920, **28**, 339.)

X-ray therapy during the last few years has made new progress, thanks to new high-tension apparatus and to new, more resisting, and better regulable tubes, as well as to new methods of technique. Rutherford, with a Coolidge tube functioning under 200 kilovolts, has obtained rays traversing 1 cm. lead. The residual irradiation after this filtration was practically homogeneous and nearly equal in hardness ($\lambda = 0{\cdot}06$ Angström) to the gamma rays of radium.

In several German clinics there are now apparatus functioning under 200 to 220 kilovolts, such as the 'Intensiv Reform' of Weifa, of Frankfort, and the 'Symmetry' of the Maison Reiniger of Erlangen, the 'Multivolt' and the 'Radiosilex' manufactured by Siemens. At Prof. Gauss's clinic at Fribourg is an 'Intensiv Reform' of 300 kilovolts. The principle of these apparatus consists of transformers placed in series with wave selectors or special valves. In Italy, Bobbio and Cardolle, of Turin, and Balzarini and Gorla, of Milan, construct similar apparatus. To work with these tensions specially constructed X-ray bulbs are necessary, whether for gas (Muller's 'Siederröhre', Gundelach's 'Constant' functioning with Wintz's automatic regulator), or for thermo-ionic current (Coolidge, with very long electrodes and Lilienfeld's tube).

Dessauer, Wintz, Warnekros, and Lilienfeld have tried to establish the technique of deep therapy with these new apparatus. Doses have been studied biologically with Szilard's iontoquantimeter. Among radiotherapeutic factors (intensity, voltage, distance, thickness of the filter, surface) the filter is the most important. Filtration should be quite 10 mm. aluminium or ½ mm. zinc, so as to lessen the error between superficial and deep doses. To determine the duration of application a biological measure must be used, that of the erythema dose being DE. According to Wintz the DE obtained with a filter of 0·5 mm. zinc consists of a redness of the skin which appears eight to ten days after irradiation, and leaves a simple pigmentation for four or five weeks; except for nephritics DE is always the same. This dose corresponds to 25 to 27 H, under the filter, on the skin. Still, according to Wintz, if DE is given value 100, the ovarian dose provoking amenorrhoea is 34; the dose for sarcoma is 60 to 70, and for carcinoma 100 to 110; the stimulating dose for carcinoma is 35 to 40; intestinal dose, provoking ulceration, 135; dose for muscle, provoking myositis, 180.

In deep application account must be taken of dispersion and absorption, of the secondary rays, of diffusion, of fluorescence and electronics, whose important biological properties have been brought to light by Ghilarducci.

The author shows how he arrives at the ovarian dose, and this assists the determination of the number of ports of entrance, duration of the séances, and their number. Applications must be administered quickly so as to avoid auto-immunization, which would prolong the treatment. He also throws light on the problem of uterine carcinoma. Quick treatment is necessary to avoid phenomena of auto-immunization and of excitation, and periods of rest must be allowed between the series of séances which, it must be remembered, carry in their train leucopenia, hypohaematia, and hypohaemoglobinaemia.

After recalling Warnekros's method, the author describes his own with 'Intensiv Reform' and a Fürstenau-Coolidge tube. He gives a table of absorption and sets out the results obtained for haemorrhagic metritis, recurrence of vaginal cancer, for large lymphomata of the neck, and for carcinoma of the tongue. He finishes by praising the transformer of Scotti and Brioschi made by Gorla, which, he says, is ultra-powerful, furnishing 235 kilovolts (45 cm. spark-gap). S. U. L.-B.

**BÉCLÈRE, A.** La radiothérapie du cancer de l'utérus à la clinique gynécologique d'Erlangen. [**The radiotherapy of carcinoma of the uterus at the gynaecological clinic at Erlangen.**] *J. de radiol. et d'électrol.*, 1921, **5**, 10.

The researches of Seitz and Wintz are of great interest from very different points of view. From a scientific point of view they are based on as exact a measurement as possible of the dose received at the surface, and the laborious determination necessary to kill the cancer cells at a depth. From a practical point of view they have met with remarkable success.

**Method of dosage.** Seitz and Wintz followed Villard and Krönig and Friedrich. They only used very penetrating rays obtained with a spark equivalent to 35 to 40 cm. and filtered by a sheet of zinc 0·5 mm. thick, equal to 11 mm. of aluminium. They have determined the 'Erythemdosis' or 'erythema dose', and use that as a standard measurement under the name 'Hauteinheitdosis' or unit of 'cutaneous dose'. The 'Karzinomdosis' or 'cancer dose' is equal to 110 per cent. of the unit of cutaneous dose: it corresponds to 37 discharges from their iontoquantimeter.

**Determination of the lethal dose for cancer.** In the first place they found that a dose corresponding to 42 discharges from the iontoquantimeter, given at a single sitting, was certain to cause the complete disappearance of a neoplasm. This caused a radiodermatitis of the first or second degree. Later researches carried out on superficial carcinomata and carcinoma of the neck of the uterus led them to use a dose of 37 discharges, that is, 110 per cent. of the unit of cutaneous dose.

**Method of irradiation of uterine carcinoma.** An account of a series of experiments is given, the object of which was to determine the method of giving a lethal dose of irradiation to the neck of the uterus without damaging the skin. They found that a port of entrance 6 cm. × 8 cm., with the bulb 23 cm. from the surface of the skin, was the most favourable. Three ports were used anteriorly and three posteriorly, one in the middle line and one on either side. Through each port the rays ought to reach the neck of the uterus exactly, to make sure of this a special tube was used holding a small fluorescent screen at 45° to the axis of the tube: this was passed into the vagina. These researches showed that the dose received by the neck of the uterus was, on an average, 23 per cent. of the superficial dose through the median anterior port, 20 per cent. through the lateral anterior and median posterior ports, and 15 per cent. through the lateral posterior ports. If needs be, the vulvar region can be employed as a seventh port; through this an additional 20 per cent. of the superficial dose can be applied to the neck of the uterus. Thus by using six ports a total of 110 per cent. of the unit of cutaneous dose can be applied to the neck of the uterus without injuring the skin. To avoid an insufficient dose they give 120 per cent. of the unit of cutaneous dose.

**Technique of treatment.** The patient must be prepared. The positions of the six ports are then fixed. The essential point is that above each port of entry the localizing tube with the X-ray bulb above it should be placed in such a manner that the axis of the cone of rays passes through the neck of the uterus. This is not always a simple matter. The strength of the current through the X-ray bulb is not usually greater than 2·3 milliamps. Under the conditions given, the time necessary for the skin to receive a unit of cutaneous dose through one of the ports of entry is from 33 to 40 minutes: usually the time given is from 30 to 33 minutes, that is, 3 to 3½ hours in all. They give as a routine at the beginning of the irradiation an injection of morphia, often accompanied by $\frac{1}{20}$ gr. of scopolamin.

**Discomforts and dangers of treatment.** The commonest occurrence is that of sickness of penetrating radiations as the author describes it. The symptoms of this are then given; among them is the effect on the blood, from which it was concluded that six weeks should elapse between sittings. A lethal dose for carcinoma should always be given in a single dose, therefore the discomforts cannot be overcome by giving treatment on two successive days. Patients showed the discomforts and dangers inseparable from this method of treatment the same as they would those of a surgical operation.

**Radium therapy and X-ray therapy combined.** When employing radium therapy alone for cases of cancer of the neck of the uterus Seitz and Wintz used to give 3,000–3,500 mgm. hours of radium element, but in their combined treatment they only give 1,200–1,800 mgm. hours using 100–150 mgm. of radium bromide suitably shielded which is inserted into the cervical canal for 24 hours. Occasionally after six weeks a second dose for 12–24 hours is needed. The patients are also X-rayed.

**X-ray therapy alone and X-ray Wertheim.** From the results they obtained in a certain number of cases they were led to believe that Wertheim's operation combined with X-ray therapy in cases of carcinoma of the neck of the uterus was the best treatment. Since January 1918 this is the only form of treatment they have used.

**Macroscopic and microscopic changes of the lesions treated.** With radium alone the macroscopic changes are rapid and early; with X-rays alone these changes are slow and late. Microscopically there is no essential difference in the cells, but as regards time the changes are the same as above.

**Criticisms and conclusions.** Béclère criticizes the use of the same iontoquantimeter for radiotherapy and radium therapy, and regrets that known and commonly used units were not employed, also that an exact measurement of the difference of tension between the two electrodes was not made instead of using a spark equivalent to 37 cm. He also notes that no difference in dosage was made when treating different types of carcinoma, and says that the treatment of carcinoma of the uterus is not certain yet as stated by Seitz and Wintz. He agrees that speaking generally the knife will give place more and more to penetrating rays, and that the combination of internal and external penetrating radiations will appear more and more necessary. The technique of the radium therapy is very good, but the author prefers that of Regaud; the researches of Seitz and Wintz will go far in perfecting the technique of peripheral X-radiation.

P. L.-B.

## *Radio-technique*

**Failla, G. Radium technique at the Memorial Hospital, New York.** *Arch. of Radiol. & Electroth.*, 1920, **25**, 3–19.

Emanation or active deposit of radium is used, never the salt itself. The latter, dissolved in acidulated water, is kept in a vault and the emanation pumped off every morning. As the water is decomposed by the radiations, the emanation has to be purified: the process used is that of Duane and Debierne.

The emanation is sealed in glass tubes of two stock sizes: (1) 0·6 mm. diameter and 10–15 mm. long contain 100–250 or even 400 millecuries of emanation when first made; (2) 0·3 mm. diameter, 3 mm. long contain 1–4 mc. The stronger tubes are put into silver tubes 0·5 mm. thick and 16 mm. long.

The filters used are 1·5 mm. and 1 mm. of platinum, 2 mm. of lead and 0·5 mm. of silver, 0·5 mm. and 0·2 mm. of aluminium. Filters, such as rubber, wood, &c., are used in making the applicators.

**The use of dental compound applicators.** The dental modelling is softened in hot water, applied over the lesion and moulded into the desired shape. When cold it is removed and in the area to be treated, deep grooves are cut. Silver tubes containing the requisite amount of emanation are placed in the grooves, which are then filled with paraffin. The applicator is then placed upon the lesion for the requisite length of time. The advantage is that the radio-active source is distributed exactly as desired, and remains in the same position throughout.

The dose is specified in mc. hours per sq. cm. of surface treated, and the amount of emanation and the area are stated. The tubes are sunk in the mould about 3 mm. from the surface, with at least one tube per sq. cm. of projected area. The filter is 0·5 mm. silver plus 2–3 mm. paraffin. Provision is made for the protection of normal tissue. Effective doses range from 40–60 mc. hours per sq. cm. If there is considerable cross-firing the smaller dose should be given.

**Uses of bare tubes.** During the last two years many patients have been treated by inserting small emanation tubes into the growth by means of a steel trocar, and allowing them to decay *in situ*. This is more effective than the use of steel needles with a tube of emanation at the end. In the former method a small dose for a long time is used in contrast to a larger dose for a shorter time in the latter method. The bare tubes cause no discomfort; are distributed throughout the mass; are innocuous after the emanation has decayed, and can be used in sites where the prolonged application of the steel needles is impracticable.

The most important points are:—

(1) The tubes should not contain more than 4 mc. of emanation each, preferably 1–2 mc. or less.

(2) Tubes should not be placed too near healthy tissue.

(3) Tubes should never be placed near large arteries, veins, or nerve trunks.

(4) Great care should be taken in treating lesions near bones or in thin-walled organs.

(5) The total amount of emanation used depends on the size, location, and pathological nature of the lesion. Roughly, the average dose is about 0·5 mc. per c.c. of tumour.

**Gamma-ray applicators.** One applicator is a flat box 7 × 10 cm., in which many silver tubes can be placed. The bottom is lined with 2 mm. of lead. Seventy-two tubes can be used, making up a dose of 3,000 mc. if desired. Ordinarily the amount used varies from 1,000–2,500 mc. This pack is usually placed from 4–10 cm. from the skin. The doses vary from 10,000 mc. hours at 6 cm. to 18,000 mc. hours at 10 cm. In general it is used for large, deep tumours and combined with the bare tube method.

If localized treatment with penetrating rays is desired, a dental compound mould is made to which is attached a lead tray 2 mm. thick. The distance varies between 2–4 cm. according to the thickness of the dental compound between the surface of the lesion and the tray. The radiation is very penetrating. Another applicator is a block of wood 4 × 4 × 6 cm. One side 4 × 6 cm. is lined with 2 mm. of lead; the other is not. The other four sides are covered with 3 mm. of lead. The silver tubes are placed on the 2 mm. face, and held by adhesive tape and covered by a lead cap. When applied, the face not lined by lead is placed next to the skin. The wood absorbs secondary radiation from the lead.

**Special applicators.** For uterine cases a thin cup of iron with 2 cm. of mercury, designed by Bailey, is used; on top of this is a lead block which receives the tubes, these are covered with 1 mm. of aluminium, and the whole held in place by an aluminium screw cap. This gives a beam of gamma rays mainly forward so that the surrounding tissue is not unduly affected. The usual dose is 1,000 mc. for three hours or 3,000 mc. hours applied as follows:—1,000 mc. hours with the applicator pressed against the cervix and pointing straight forward; 1,000 mc. hours directed towards the left parametrium and 1,000 mc. hours directed towards the right parametrium. The filtration forward is 0·5 mm. of silver, plus 1 mm. of platinum, plus 2–3 mm. of aluminium. The average distance from the cervix is 1 cm. The object is to reach the outposts of the disease rather than to destroy the cancer cells in the cervix; these can be otherwise dealt with.

Bailey's method is as follows:—cervical treatment of 1,000–2,000 mc. hours, the emanation being in a 1 mm. platinum tube covered with rubber. A similar tube is inserted into the uterine canal to treat the neck and body, the dose being 1,500 mc. hours. Cross-firing is used to irradiate the parametrium. The lead-lined block is used to give a total of 18,000 mc. hours through six skin portals around the pelvis.

Janeway treats the local lesion by burying emanation tubes to the extent of 20–40 mc. in all. In addition, three platinum tubes 1 mm. thick, covered with rubber are inserted in the utero-cervical canal, giving a dose of 3,000 mc. hours. If the fundus is involved the abdominal pack 10 cm. from the skin is used giving a dose of 20,000 mc. hours.

For cancer of the bladder steel helices are used through the sheath of a Brown-Buerger operative cystoscope. If the carcinoma is limited and the limits can be seen (1) 500–1,000 mc. of unscreened radium is passed into the bladder and held against the tumour. The largest dose given thus has been about 650 mc. hours. (2) When there is no danger of perforation there may be a steel needle at the end of the flexible instrument which is inserted into the base of the tumour. Doses of 100 mc. hours or 50 mc. for two hours have been given. (3) The same instrument, with a suitable plunger, may be used to insert bare tubes.

For extensive tumours, especially round the neck of the bladder, two silver capsules 0·5 mm. thick covered with rubber tubes 1 mm. thick and attached to linen threads are passed into the bladder and left there with the threads in the urethra. The usual dose is 800 mc. hours or 100 mc. for 8 hours. The tubes are removed by the linen thread.

Carcinoma of the prostate has been treated by steel needles inserted through the perineum or by the bare tube method. Dose for steel needles 50 mc. for 12 hours: for the bare tube method, 3–5 mc. in several tubes.

P. L-B.

# MEDICAL SCIENCE

## ABSTRACTS & REVIEWS

Volume IV. Number 4 July 1921

## CONTENTS

REVIEWS: PAGE

INFLUENZA . . . . . . . . . . . . . . . . 295

DISEASES OF THE RESPIRATORY SYSTEM . . . . . . . 309

THE CAROTID AND VERTEBRAL ARTERIES: HAEMORRHAGE AND ANEURYSM: CEREBRAL THROMBOSIS AND EMBOLISM 322

NEUROSYPHILIS . . . . . . . . . . . . . . . 335

ABSTRACTS:

SURGERY . . . . . . . . . . . . . . . . . 341

NEUROLOGY . . . . . . . . . . . . . . . . 347

PATHOLOGY AND BACTERIOLOGY . . . . . . . . . 352

BIOCHEMISTRY . . . . . . . . . . . . . . . 376

RADIOLOGY . . . . . . . . . . . . . . . . 388

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# REVIEWS

## INFLUENZA

**Epidemiology.** According to Böhm, the course of the 1918 influenza epidemic in Vienna was decidedly more severe than that of the previous epidemic in 1890–93. In the second six months of 1918 4,008 deaths were certified as due to influenza. As of the 4,154 deaths from disease of the lungs and pleurae during this period, 2,878 could be attributed to influenza, after subtracting the normal average of deaths due to these diseases, there were in all 6,886 deaths due to influenza during the second half of 1918, while the number of deaths due to tuberculosis during the same period was only 4,305. In 1919 there were 533 deaths from influenza and 2,904 deaths from diseases of the lungs and pleurae. In January 1920 the number of deaths from influenza rose again, 1,011 deaths from influenza and 1,794 deaths from diseases of the lungs and pleurae being certified from January 1 to May 1, 1920, so that, according to the previous calculation, 2,279 deaths could be attributed to influenza. The Vienna epidemics of 1918 and 1920 were connected by an endemic which was observed throughout 1919. The epidemic of 1918 rose rapidly and fell rapidly, while the epidemic of 1920 rose gradually and gradually subsided. In 1918 the disease attacked a population which had been free from influenza for many years, whereas in 1920 a large proportion of the population had already had an attack of influenza and was therefore immune, while the virulence of the causal agent had been already weakened by the endemic of 1919. The character of the two epidemics was therefore different. In the epidemic of 1918 severe haemorrhagic pneumonia predominated, whereas in 1920 the attacks were milder on the average and frequently appeared in the form of nervous disturbances and in isolated instances as severe encephalitis.

As regards the distribution of the fatal cases according to sex, age, and social position, Böhm states that males and females were almost equally affected, and that in 1918 principally young and often very vigorous persons were attacked (72·2 per cent. of the deaths occurred in persons between 10 and 40), while in 1920 a large number of children and persons in advanced life were the victims, only 51·2 per cent. being between the ages of 10 and 40. In striking contrast with the tuberculosis mortality the well-to-do districts of Vienna showed as high or even higher mortality from influenza than the poorer districts.

From their observations of the influenza epidemic of 1920 at the Hôpital Necker, where 141 cases occurred with 15 deaths, Rénon and Mignot found that unlike the pandemic of 1918–19 which principally attacked the young and vigorous, the outbreak of 1920 attacked all ages and constitutions. A third of the patients were over 40, and some were between 70 and 80.

The disease, however, remained relatively mild compared with the epidemic of the previous year.

Petrén quotes the following figures given by Bloch representing the number of deaths from influenza in the towns of Sweden (with a population of about 1,650,000) during the different months of the 1918 epidemic: July, 29; August, 321; September, 728; October, 3,318: November, 2,200; December, 1,175. Poliomyelitis, which was stated by Horder to be more frequent than usual in December 1918, did not show any such unusual frequency in Sweden.

In Matthiasson's account of the recent epidemic of influenza in Iceland, the most interesting feature is his claim that, by quarantine measures, the disease was confined to the south and west, and that half the population of the country was thereby protected from the disease. Before the outbreak of the epidemic in Reykjavik, where it ran a highly virulent course, there had been sporadic outbreaks for two or three months of a comparatively benign and but little infectious, influenza-like disease. Again, a few months after the influenza had passed away, there was another mild, influenza-like epidemic which swept over the whole country, but was chiefly confined to children. In this connexion Matthiasson observes that 2 to 7 months after each of the three epidemics of influenza in 1890, 1894, and 1900, catarrhal epidemics broke out among children, related to, and probably conferring immunity to, genuine influenza.

Bassett-Smith remarks that the epidemics of influenza which occurred in the Navy in 1918–19 were similar in many respects to those which occurred on shore, but the close proximity of cases in barracks and ships tended to make the spread of infection more easy than in many other places. In the spring epidemic the general character of the disease was mild, but the sudden invasion, often accompanied by collapse, was very typical. The total number of persons who contracted the disease was 10,313 out of 90,000 officers and men in the Grand Fleet. There were 16 cases of pneumonia and 4 deaths. During the whole year of 1918 the total number of cases of influenza recorded from home and foreign stations was 80,144. This yielded a total of 396,861 days' sickness (excluding the time spent in hospital) or an average of 4·9 days from each case on board, with 2,322 deaths, or a mortality of 2·94 per cent. The percentage mortality was much greater in the autumn than in the spring epidemic. At one depôt in the first epidemic there were 928 cases and no deaths, whereas in the winter, with 468 cases, there were 14 deaths or a mortality of 3·01 per cent.

For further information concerning the epidemiology of the pandemic of influenza of 1918–19 reference should be made to the recently published report issued by the Ministry of Health.

**Aetiology.** Engelbreth records his experiments with transmitting influenza through fleas. Positive results were obtained in 7 out of 14 cases. The source of infection in all cases was a department for influenza where all the patients had typical attacks, in many instances complicated by pneumonia. The incubation period in the positive cases was 1–2 days, and in one case 3 days. With one exception, in which the disease was complicated by pneumonia, the attack produced was mild and uncomplicated.

**Blood.** Harry investigated the blood in 65 cases admitted to the Hamburg-Barmbeck Hospital with the diagnosis of influenza. Of these 10 had to be excluded as they were found to be suffering from another disease or to have another disease as well. His conclusions were as follows: (1) In mild cases there is a leucopenia and relative lymphocytosis, the eosinophils are entirely absent or much diminished, and the mononuclears and transitionals usually increased; (2) in complicated cases there is hyperleucocytosis and relative polymorphonuclear leucocytosis. The eosinophils, mononuclears, and transitionals are the same as in the mild attacks; (3) after the temperature has become normal the leucopenia is replaced by leucocytosis, the lymphocytosis persisting until finally a normal count is re-established. Hyperleucocytosis lasts for a short time after the temperature has become normal, and the relative polymorphonuclear leucocytosis is replaced by a relative lymphocytosis, but a normal count is soon re-established; (4) the extension of a broncho-pneumonic process is shown by an increase in the polymorphonuclears and leucocytes, which is thus a guide to prognosis. Harry attributes the conflicting results obtained by various observers to the cases investigated not having been pure influenza and to the tendency to diagnose every febrile catarrh as influenza in epidemic times.

As the result of the examination of 31 cases of influenza, 10 of which were uncomplicated and 21 complicated by pneumonia, Stoichitia came to the following conclusions: (1) In mild and uncomplicated cases there is a leucopenia and a normal number of leucocytes is exceptional; (2) in mild cases complicated by pneumonia there is a slight leucocytosis; (3) in severe cases of pneumonia there is a hyperleucocytosis which may become very marked; (4) in cases with grave clinical symptoms such as bilateral broncho-pneumonia, leucopenia is an unfavourable sign.

Milio, of the Palermo University Institute of Clinical Paediatrics, examined the blood of 20 children suffering from influenza with the following results: (1) Both in simple and complicated forms there was a slight diminution in the haemoglobin and red cells; (2) in uncomplicated forms there was a leucopenia with diminution of the polymorphonuclears and an increase of the lymphocytes in 75 per cent. of the cases, the number of leucocytes remaining normal in 25 per cent. In complicated forms there was a leucocytosis and polymorphonucleosis in 70 per cent., and even in the cases in which the total number of leucocytes remained normal there was a relative increase of polymorphonuclears; (3) the viscosity of the blood as determined by Hess's viscometer was not affected; (4) the coagulability of the blood determined by Wright's method was normal.

**Symptomatology.** The occurrence of *chronic lung disease following influenza* and simulating tuberculosis in its frequent localization at the apices and in general symptoms, especially subfebrile temperature and night sweats, has been recently discussed by Hildebrandt and Treupel in Germany, Furno in Italy, and Radin in the United States. Hildebrandt uses the term 'chronic influenza' for the morbid processes lasting for months for which *B. influenzae* is responsible, whether anatomical changes are present or not. He maintains that influenza should be regarded not only as an acute, but also as a chronic infectious disease, and the most important affection of the respiratory organs next to tuberculosis.

Treupel, whose experience agrees with that of Hildebrandt, states that the condition, both in its clinical and X-ray appearances, bears the closest resemblance to certain forms of tuberculosis, and that the two conditions may sometimes coexist. He records the case of a woman, aged 62, who had a pulmonary abscess for 28 years unaccompanied by symptoms, and dating from an attack of influenzal pleurisy.

Radin records 12 cases of chronic lung disease following influenza. In

3 cases the duration of the disease was over 1 year, in 2 cases 11 months, in 5 cases 10 months, and 2 cases about 8 months. The lesion present was in 6 cases pleurisy, in 3 cases chronic diffuse bronchitis, and in the remaining 3 pulmonary tuberculosis. In all but the 3 tuberculous cases the pathological process was at the bases of the lungs. Sputum was absent in the pleurisy cases as a rule, and copious in the bronchitis cases. The pain occupied wide areas, localized pain occurred only once. Fever was absent altogether.

Furno states that chronic post-influenzal broncho-alveolitis occurs in subjects of all ages and both sexes of normal and even robust constitution without tuberculous antecedents, whereas tuberculous broncho-alveolitis as a rule attacks persons with a poor constitution who often have a previous history of tuberculosis.

Legrand and Auguste record the case of a man, aged 50, who on the fourth day of influenzal pneumonia developed within 24 hours a *seropurulent effusion* in the left pleura. 24 hours later it was completely absorbed, and 2 days afterwards an equally large effusion was found on the opposite side and was also absorbed in the course of a few days without thoracentesis. Another remarkable feature in the case was the aseptic character of the fluid of both effusions. Although a turbid fluid was obtained by puncture containing numerous polymorphonuclears, a few lymphocytes, and red cells, no organism could be found either on direct examination or in cultures.

In the course of autopsies on cases of influenza during the summer and autumn of 1918, Catsaras, of Athens, was struck by the frequency of *fatty embolism* in the lungs, which he found in 18 out of 67 lungs examined. He considers that this embolism may account to some extent for the intense dyspnoea in cases where the pneumonic foci are not extensive, and possibly for some of the sudden deaths when there are very extensive fatty emboli in both lungs. He suggests that the large amount of fat absorbed by the lacteals and portal vein as the result of a prolonged milk diet has not been retained in the liver but has passed into the hepatic veins and thence into the lungs.

In examination of cases of influenza, whether complicated by pneumonia or otherwise, Kirch has occasionally found more or less well-marked dullness in the region of the anterior mediastinum. The supposition that the dullness was due to *enlarged mediastinal glands* was confirmed by an autopsy on a fatal case.

Müller, of the Hamburg University Pathological Institute, and Kleberger, of the Kaiser-Wilhelms-Academie, Berlin, each record a fatal case of influenza complicated by infection with *Aspergillus fumigatus*. The cases are of interest in that most of the pneumonomycoses hitherto observed have been chronic diseases, which have been occasionally associated with tuberculosis in their later stages. Kleberger suggests that the chronic disease that sometimes follows influenza may be due to *pneumonomycosis aspergillina*.

Cases of post-influenzal *myocardial involvement* in which the auricle and conduction pathways of the heart were particularly affected are recorded by W. W. Hamburger, of Chicago, who offers the following classification of post-influenzal cardiac complications: (*a*) Fatal cases showing acute parenchymatous degeneration and vacuolization of the myocardium; (*b*) non-fatal, acute cases showing involvement of the auricle and conduction system during the height of the infection with complete restoration to the normal on subsidence of the infection. Duration 2–6 weeks; (*c*) non-fatal chronic cases with arrhythmia and involvement of the auricle persisting and causing partial invalidism long after subsidence of the acute infection. Duration 12–17 months or more.

Lederer, of the German Pathological Institute at Prague, records a fatal case of *pseudo-membranous oesophagitis* in a male infant aged 1 month and 17 days, whose mother had died of influenza two days after confinement. In addition to gastro-entero-colitis and broncho-pneumonia, the autopsy on the infant showed a membranous and necrotic oesophagitis from which *B. influenzae* and *Streptococcus mucosus* were grown in large quantities as well as a Gram-negative bacillus apparently allied to *B. fusiformis*.

*Jaundice* is generally regarded as a rare and ominous symptom in influenza, though a few writers hold an exactly opposite view. During the epidemic of 1918–19, Reiche (1) saw 9 cases of severe jaundice without discoloration of the stools and 7 mild cases. 7 of the cases ended fatally. Corinaldesi, of the Genoa University Medical Clinic, records a case of post-influenzal jaundice in a man, aged 34, which persisted for 5 months until laparatomy was performed. No evidence of calculi or thickening of the duodenum or pancreas was found, and gradual improvement ensued until complete recovery took place.

Lowe records three fatal cases of extensive membranous *colitis* complicating influenzal pneumonia with septicaemia. Alimentary symptoms were practically absent in each of the cases, and any marked pathological condition of the gut was not anticipated from the slight clinical symptoms observed.

**Renal complications.** According to Petrén the renal affection in influenzal pneumonia, though very frequent, is not severe, and even in cases in which a large quantity of albumin was present in the urine he found that the complication was of a mild character. Klemperer also maintains that the prognosis in influenzal nephrosis is good, even when there is much albuminuria, and that simple methods of treatment, such as rest in bed, milk diet, and sweating, are usually sufficient.

During the last four epidemics of influenza, from 1918 to 1920, Goldberg has seen 30 cases of influenzal haematuria, so that he has come to the conclusion that it is not so rare as is usually described. On microscopical examination of the urine it was found that the condition was not a pure haematuria but was associated with pyuria. Cystoscopy in ten cases showed a diffuse cystitis most marked at the ureteric orifices with large and small erosions. Goldberg regards the haematuria as being always due to a descending perirenal haematogenous pyelocystitis on the following grounds: (1) The absence of any periureteral source of infection; (2) the presence of albuminuria in almost all the cases before or after the occurrence of haematuria.

Izar has found acetone and diacetic acid either separately or in combination in a large number of cases of influenza. These substances were present not only in cases with visceral localizations, but also in uncomplicated cases. He is inclined to the view that some of the symptoms of influenza, such as vomiting and dyspnoea, and somnolence, when they are not due to circulatory, respiratory, and renal disturbance, are caused in part at least by acetonuria.

**Nervous and mental complications.** Ciccarelli records a case of transient poliomyelitis following influenzal broncho-pneumonia in an adult characterized by complete loss of power in the lower limbs, abolition of the knee-jerks, without any sensory changes, and followed by wasting of the muscles. The sphincters were intact. A diagnosis of acute anterior poliomyelitis of the lumbo-sacral segment of the cord was made owing to the sudden onset, rapid development, and degenerative character of the paralysis in the lower limbs. Gradual improvement took place, so that by the end of four months the patient was able to walk two miles with the help of a stick.

Urbantschitsch records a case of influenza or possibly lethargic encephalitis with bilateral choked disk and unilateral paralysis of the sixth nerve, which appeared and disappeared no less than three times before recovery took place.

According to Menninger, whose paper on influenza and nervous syphilis has previously been abstracted (vide *Medical Science*, 1919, **1**, 253), the usual effect of influenza on the brain is not the production or precipitation of hypophrenia, and if it ever produces hypophrenia it is probably by a more or less obvious encephalopathy. On the other hand, of those already showing mental deficiencies a few are affected adversely by influenza, and the symptoms of hypophrenia are aggravated. Psychoses of an indeterminate type are occasionally precipitated by influenza in the feeble-minded as in normal persons. Occasionally, though rarely, the effect of influenza on hypophrenia may be symptomatic amelioration.

**Skin.** According to Bergé and Hufnagel, skin eruptions are rare in influenza. During the 1918 epidemic Le Clerc noticed an eruption in only 10 out of 549 cases. Bergé and Hufnagel report a fatal case of influenzal broncho-pneumonia in a man aged 23, who presented an eruption of lenticular rose spots. The blood cultures were negative and the intestines did not show any lesions. Widal's reaction was not performed as the man had been inoculated several times against typhoid.

Leimdörfer regards the skin eruptions met with in influenza as an expression of a vascular lesion like the enanthem on the mucous membrane of the throat, tongue, and conjunctiva. In some cases an erythema may be observed, chiefly affecting the skin of the trunk, and the limbs only in a slight degree, and disappearing in two days' time without leaving any desquamation. Leimdörfer saw six cases of scarlatiniform eruption, usually at the height of the disease, lasting for two days and not followed by desquamation. In a small number of cases an urticarial eruption was observed affecting the forearms and hands, legs and feet.

Gioseffi states that during an epidemic of influenza in the autumn of 1919 in Parenzo, a small town in central Istria, scarlatiniform eruptions followed by desquamation were so intense as to raise a doubt as to the diagnosis of influenza. None of the cases, however, developed nephritis or suppurative cervical adenitis.

**Surgical complications.** Russell maintains that symptoms simulating an acute abdominal lesion, especially appendicitis and cholecystitis, are common in influenza, and that their frequency is not sufficiently brought out in the text-books. Although in some cases a differential diagnosis is extremely difficult, the safest procedure in doubtful cases is an expectant treatment. If an exploratory operation is decided upon, a local anaesthetic is advisable. Although occasionally a surgical abdominal lesion and influenza may coexist, the great majority of cases of influenza with abdominal symptoms have no surgical basis, but are either reflex or due to some condition which would not be benefited but rather harmed by laparotomy (cf. *Medical Science*, 1920, **2**, 425).

Neumann and Zoepffel record a case of diaphragmatic pleurisy simulating perforative peritonitis in a man aged 39. Laparotomy was performed, but nothing was found in the abdomen. Subsequently pneumonic foci were found in the lower lobes of both lungs, accompanied by high fever, cyanosis, and herpes labialis, and followed by a turbid serous pleural effusion containing haemolytic streptococci. Death took place on the thirteenth day. The case shows that influenza may commence with diaphragmatic pleurisy which may closely simulate perforation of a gastric ulcer. The writers suggest that in such cases slight cyanosis of the face and injection of the palate may indicate the presence of influenza.

A case of osteomyelitis of the hyoid bone as a sequel to influenza is reported by Lotsch in a man aged 44. Suppuration persisted for several months, but recovery took place after removal of the sequestrated right thyro-hyal cornu.

Baudrimont records a case of bilateral hygroma of the prepatellar bursa in a woman aged 41, following a mild attack of influenza.

Coulet reports a fatal case of *tonsillar abscess*, probably of influenzal origin, in a previously healthy and vigorous young man of 20. Death took place within four days as the result of mediastinal infection, and the autopsy showed an abscess in the right tonsil, cellulitis of the neck, and sero-purulent pleurisy with marked degeneration of the pericardial sac.

According to Canuyt, who records an illustrative case in post-influenzal *ulceration of the larynx*, the vocal cords are exclusively affected. The ulceration is situated on the free border of the vocal cord, most frequently on its posterior third, and rarely on the anterior third. The ulceration is often symmetrical, but is more marked on one side than the other. There is never any peripheral infiltration as in epithelioma or gumma.

Bittorf records four cases—three in men and one in a woman—in which influenza was complicated by *symptoms of Ménière's disease* of apoplectiform onset but without disturbance of hearing, and manifested by violent headache, vertigo, nausea, vomiting. and nystagmus. The symptoms lasted from six days to seven weeks. In protracted cases lumbar puncture had a good effect. The condition was most probably due to toxic irritation of the vestibular nerve.

Danis, of Brussels, records a case of inflammation of the cellular tissue of the right orbit, following influenzal pneumonia, in a soldier aged 34. Thrombophlebitis of the retinal vessels and atrophy of the optic nerve supervened, owing to an extension of a thrombophlebitis of the orbital vessels to the retina.

**Influenza and tuberculosis.** Fishberg and Boas, the former of whom has published two previous papers on this subject (vide *Medical Science*, 1919, **1**, 162; 1920, **2**, 233) report an outbreak of influenza in the tuberculosis pavilion of the Montefiore Hospital, New York, during January and February 1920, 28 out of 127 patients being affected. This proportion seems to be about the same as might be expected among non-tuberculous individuals. The clinical form of tuberculosis and the stage of the disease had no influence on the liability of the patients to contract influenza. Of the 28 patients who developed influenza 9 died, which is a higher mortality rate than is generally observed. 22 of the 28 developed broncho-pneumonia, which is also a much higher rate than usual. The writers, however, believe that the liability to broncho-pneumonia varies with the epidemic, as in 1918 a smaller proportion of their patients developed it and the mortality was lower. The clinical course of influenza resembled that in the non-tuberculous. The liability to develop broncho-pneumonia bore no relation to the size, clinical form, or acuteness of the tuberculous process in the lungs or pleurae. In nearly all the patients who recovered the influenza had no appreciable effect on the lung lesion as far as could be discovered by physical examination of the chest or the subsequent course of the disease.

On the other hand, Lortat-Jacob states that he has seen several cases of latent tuberculosis which started with pleurisy take on a rapid and often fatal course as the result of a superadded influenzal infection.

Kieffer's investigations show that out of 274 cases admitted to the Lung Hospital in Mannheim between December 1, 1918, and June 1, 1919, there were 55 in which the pulmonary disease had developed in connexion with an attack of influenza. Most of these patients were young adults who were well developed and showed no sign of the phthisical physique. Only in 12 cases was there a history of glandular tuberculosis, pleurisy, or persistent bronchitis, and a family history of tuberculosis was seldom obtainable. The disease in these cases ran a rapidly progressive course, and frequently there was an interval of only a few months between the onset of the influenza and death from tuberculosis. But what distinguished these cases more than anything else from the non-influenzal cases of pulmonary tuberculosis was the X-ray picture which almost invariably showed the tuberculosis to originate about the hilus. The X-rays often showed massive, tumour-like hilus shadows, which were in some cases unilateral, and in others bilateral, and which did not as a rule merge into the shadows cast by the lungs. Indeed, in 'pure' cases the surrounding lung tissue seemed perfectly normal, and the picture was that of hilus tuberculosis in childhood. But in most cases there were more or less extensive shadows radiating out from the hilus into the lungs, and in advanced cases these radiating shadows were so large and numerous as to obscure the original hilus shadows. The involvement of the apices of the lungs was comparatively late, to judge by the X-rays. In contrast to this malignant type of post-influenzal tuberculosis developing in previously healthy persons, Kieffer notes that when influenza is grafted on to an already established tuberculous process, the influenza itself runs a comparatively mild course, and the tuberculous disease is seldom aggravated.

Saxtorph's paper bears out Kieffer's contentions in practically every respect. Of 240 patients admitted to Nakkeböllefjord Sanatorium in the period January 1, 1919–November 1, 1919, 97 had suffered from influenza, and of these 59 had shown no sign of tuberculosis before they contracted influenza. Though these were early cases, judged by time, only 20 were in the first stage, while 15 were in the second stage, and as many as 24 were in the third stage of the disease. Saxtorph believes that reactivation of hilus tuberculosis is the cause of a clinical picture commonly seen after influenza. The patient complains of lassitude, night sweats, and cough ; his temperature is slightly raised, but the chest signs are indefinite. A skiagram, however, shows definite enlargement of the hilus glands.

Milman reports a case of tabes mesenterica in a boy aged 7, following influenza, recovery taking place after laparotomy.

**Influenza and syphilis.** From his own observations and inquiries from others, Neuda has found that as a general rule influenza runs a mild course in syphilitic subjects, and that in a large percentage of cases the Wassermann reaction in the blood becomes negative after influenza, in spite of a relatively short period of treatment, although the goldsol reaction in the cerebrospinal fluid is not affected.

From a study of influenza in syphilitic women, Strassberg has also observed that the course of influenza is not unfavourably affected by coexisting syphilis, and that on the other hand influenza has a decidedly beneficial action on syphilis, especially in a serological respect. Strassberg, however, emphasizes the fact that influenza has no effect upon the course of syphilis or the Wassermann reaction in the absence of antisyphilitic treatment, but exercises a favourable action even if the previous treatment has been slight. He suggests that the favourable effect of influenza, like that of protein-therapy, on syphilis is due to its febrile element. The fever of influenza, however, has a much more intense action than the artificial rise of temperature caused by protein-therapy. It seems that in influenza, as in erysipelas, typhoid fever, &c., processes take place which render the system unsuitable for syphilis and make it susceptible to antisyphilitic treatment, while, on the other hand, syphilis has apparently an inhibitory action on influenza.

**Influenza in children.** Hamburger and Bálint, of the Berlin University Children's Clinic, maintain that pandemic influenza in children is a formidable disease. In addition to broncho-pneumonia, in which the areas tend to become confluent, pleurisy is a frequent complication. A large number of the severe cases show toxic symptoms. The disease appeared to be worst in rickety children, and patients with severe rickets invariably succumbed. All possible methods of treatment were employed without much success.

In a paper on the influenza epidemic at the Erlangen University Children's Clinic, Jamin and Stettner state that the sexes were almost equally affected. The female sex, however, offered less resistance to the influenzal virus, and was therefore more subject to broncho-pneumonia, and showed a higher mortality. Contrary to the general rule that in adults it was the most vigorous persons who succumbed, in children the great majority of the severe and fatal cases had some constitutional weakness or recent disease, especially pneumonia. With regard to the symptomatology of influenza in childhood, certain age-periods showed an unmistakable disposition to various manifestations of the disease. Epistaxis was not observed until after the third year, while tracheal stenosis only occurred up to the third year. Infants showed a severe loss of nutrition. In early childhood, respiratory complications were specially dangerous and obstinate. Infants who had already had some other infection or shown some disturbance of nutrition were in greater danger than other children.

**Influenza in old age.** According to Thewlis (1), old age with its debility predisposes to influenza which often proves fatal. The danger of influenza in old age is due to the tendency of the disease to develop into pneumonia and the serious complications which often follow. Convalescence is slow, even if there are no complications. Lastly the diagnosis of influenza in the aged is difficult, as the disease may not present classical symptoms.

**Immunity.** Dopter has collected a large quantity of epidemiological and experimental evidence showing very definitely the acquisition of immunity after one attack of influenza. This applies, however, only to influenza itself and not to its complications, which during an epidemic may be contagious in themselves without any influenzal substratum. Although the immunity does exist, it is not absolute, as Beveridge and Cummins observed second attacks in 20–23 per cent. of their cases. As regards the duration of the immunity, according to observations made by Malone in India, it lasts at least nine months and possibly longer.

As the result of his observations in recent epidemics, Falcioni comes to the following conclusions: (1) It was only families who escaped an attack of influenza in 1918 and 1919 who contracted the disease in 1920; (2) numerous individuals and even entire families who had been attacked in earlier epidemics did not contract the disease again, although they remained in constant contact with the patients. Though he admits that there may be exceptions, perhaps more apparent than real, he maintains that post-influenzal immunity is usually of very long duration rather than limited to months, a year, or a little more.

On the other hand, according to Reiche (1), who records his experience of the influenza epidemic of 1918–19 at the Hamburg-Barmbeck General Hospital, post-influenzal immunity, if it does occur, must be of very short duration. Of 669 patients under his care 10 had two attacks and 2 three attacks in the course of a few months, the later infections being by no means always particularly mild, but sometimes remarkably severe. The average duration of the interval between the two attacks was ten weeks, the shortest period being four weeks. In a subsequent paper Reiche (2) states that of 216 cases under his care in the epidemic of January 1920, three had previously had a severe attack, one in 1918 and two in 1919, so that even a severe attack does not confer an immunity of long duration.

Chauffard found that of 40 patients, 22 of which were men and 18 women, who developed influenza between October 1919 and February 1920, 11 or 27·5 per cent. had had a previous attack during the epidemic of 1918–19. The percentage of second attacks among the men was 36 as compared with 16 per cent. among the women, which was probably due to the men being much more exposed than women to the injurious action of cold and climactic influences. Though the figures are too small to allow final conclusions, Chauffard points out that nearly three-quarters of those who contracted influenza in 1919–20 were those who had escaped in the 1918–19 epidemic. Such a proportion is an indirect proof of the immunizing action of epidemic influenza, since the new epidemic mainly attacked the small minority of persons who had escaped in the earlier epidemic, whereas the enormous number of persons who had been attacked in the earlier epidemic yielded a much smaller number of cases.

Of 178 cases observed by Treupel and Kayser-Petersen at Frankfort in November 1919, 145 stated that they had not had influenza in the previous year, and 33 had previously had an attack in 1918 or 1919.

Jaksch-Wartenhorst, of Prague, found that of 70 men and 80 women who contracted influenza in 1919–20, 20 of the men and 1 woman had had a previous attack, so that only 21 of the total 150 or 14 per cent. had had a previous attack, thus showing that influenza confers a certain though limited immunity.

Alexander and Macdonald found that of 100 consecutive cases who contracted influenza during an outbreak at Waterbury, Connecticut, in January–February 1920, only 2 gave a history of having had influenza during the 1918 epidemic.

**Prophylaxis.** Commenting on Plesch's suggestion to use inhalations of iodine vapour as a mode of prophylaxis during an epidemic by exposing plates containing a few drops of commercial iodine in offices and workshops, Cheinisse points out that such a method is far from being as harmless as Plesch declares. He alludes to the recent investigation of Luckhardt, Koch, Schroeder, and Weiland, at Chicago, which show that inhalation of iodine vapour is liable to give rise to pulmonary oedema, and that this is likely to develop much more rapidly when there is pre-existing respiratory disease such as tracheitis or bronchitis.

**Treatment.** From a study of 101 cases of influenzal pneumonia treated by the serum of convalescents, Sanborn, of Boston, concludes that this method is of value when employed during the first three days of the pneumonia, his conclusion being based on a mortality-rate of 10½ per cent. as compared with 21 per cent. in a control series of 184 cases of average severity occurring in private practice at the same period of the year in the same general locality, but not treated by serum. The value of the treatment rapidly declined when given after the third day, as shown by rapidly increasing mortality rates according as the administration of the serum was delayed from day to day. Given during the first 3 days it was three times as efficient as when delayed until the fourth day, and seven times as efficient as it was when deferred until the fifth day. Given during the first 4 days of the pneumonia it was five times as efficient as when given during the succeeding 4 days (see also *Medical Science*, 1919, **1**, 53; 1920, **2**, 430).

Földes and Hajós, of the Budapest University Medical Clinic, treated 31 cases with subcutaneous injections of 30–50 c.c. normal horse serum. 17 showed improvement after a single injection, 10 after two injections, and 1 only after the lapse of several weeks. 3 died.

Borchardt and Ladwig, of Königsberg, employed intramuscular injections of 5–10 c.c. of milk in 98 cases, most of which were severe, and frequently observed a critical fall of temperature in the next 24 to 48 hours. While admitting that caution is required in the estimation of these results, as occasionally a critical fall of temperature took place without a specific action on the disease, the writers attribute a favourable action to the milk treatment, as it was often followed by a rapid fall of temperature when other methods had failed and commencing pneumonia resolved under its influence.

Hanganut has obtained very satisfactory results in the treatment of influenzal pneumonia by intravenous injection of resorcin. The injection was often followed by a rise of temperature without aggravation of the symptoms or physical signs. The following day defervescence occurred by crisis accompanied by profuse sweating but without collapse. The resorcin was given in a fresh solution according to the following prescription: ℞ Resorcin 10 gm., Sod. chlor. 0·90 gm., Aq. dest. 100 gm., 10 c.c. intravenously. No toxic symptoms or other contra-indications to its use were ever observed. In addition to this treatment, cases of pneumonia in which resolution was delayed were given large doses of sodium citrate as recommended by Weaver and others (vide *Medical Science*, 1920, **2**, 514).

Naessens has obtained good results in influenzal broncho-pneumonia in children by subcutaneous injections of oxygen (100–500 c.c. every 2–3 hours). The immediate results were disappearance of cyanosis, diminution of dyspnoea, improvement of the pulse in strength and regularity, rise of blood-pressure, and a fall of the temperature. No change occurred in the blood picture.

Gargling with a 2 per cent. solution of chloral hydrate made by dissolving

16 five-grain tablets in 8 oz. of water is recommended owing to the antiseptic and anaesthetic action of the drug by Thewlis (2), who made an extensive use of it during the epidemic among American soldiers in France in the winter of 1918–19. The gargle is preceded by the administration of 4 gr. of calomel followed in three hours by ½ oz. of Epsom salts.

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## DISEASES OF THE RESPIRATORY SYSTEM

**Congenital absence of lung.** Levy has collected 22 cases of congenital absence of one lung, including a personal case in a tabetic man, aged 49, who died of broncho-pneumonia and uraemia at the age of 49, and states that it is the first example of the kind in almost 6,000 autopsies performed in the pathological department of the Johns Hopkins Hospital. In 15 of the 22 cases there was an absence of the left lung, and in 7 of the right lung. No satisfactory anatomical explanation has been given for this left-sided predominance, but interference with the blood-supply in embryonic life is supposed to be responsible. 12 died before the age of one year, and in 10 the period of life ranged from 8 to 70 years. Respiratory symptoms have not been common, and the patients have often come to autopsy for other than pulmonary conditions. There is a tendency for the single lung to undergo compensatory hypertrophy. The pulmonary vessels may show anomalies, but these are not constant in all cases. The primary bronchus corresponding to the missing lung is usually rudimentary, and often ends in a blind pouch. The absent lung has most often been replaced by a larger pericardial sac and sometimes by fluid, while in one case part of the small and large intestine was found occupying the left thoracic cavity. In all previous cases the chest was described as normal in contour, but in Levy's case the thorax was definitely asymmetrical, the left side of the chest being flat and the opposite side bulging. Up to the present the clinical diagnosis of absence of a lung has never been confirmed at autopsy. The case recently described by Jarisch (vide *Medical Science*, 1920, **1**, 459) is not included in Levy's series.

**Hay fever.** Walker (1), of Boston, states that although it has been well known for years that certain persons have hay fever from exposure to animals, only recently has the real causative agent been discovered and appropriate treatment instituted. The ingestion of foods and the presence of bacteria in the nasal cavities, exclusive of a definite infectious process, have likewise only recently been recognized as a possible cause of hay fever. Lastly, in some cases eye symptoms, especially conjunctivitis and possibly keratitis and a low-grade inflammation of the uveal tract, may result from eating certain foods. In those patients who have perennial hay fever due to animal emanations, food, and pollens it is usually the proteins in their substances which cause the symptoms. In the case of bacteria it may be the protein or it may be the infectious element. In testing with the animal emanations or epidermal proteins the protein and the peptone should be used separately; with the cereal grains the globulin fraction of the protein is most important; with other foods and with pollens and bacteria the whole protein seems to suffice.

Patients, when hay fever is caused by exposure to horses, may be successfully treated by repeated inoculation in gradually increasing amounts of the particular epidermal protein to which they are most sensitive. Those who are sensitive to cat hair protein may be treated similarly with equal success. In the case of hay fever caused by the ingestion of certain foods, and by the inhalation of the cereal grain flours, cutaneous tests often reveal the cause, and omission of the protein is the best treatment.

During the last five years Heermann, of Cassel, has treated nine cases of hay fever and two of nervous coryza by high-frequency currents, associated in some cases with the quartz lamp. Ten sittings, on the average, were required either on successive days or with a few days' interval between each one.

Agar has obtained good results by rubbing any fissures or sore spots found in the vestibule of the nose with an astringent lotion composed of 30 grains of silver nitrate to the ounce.

**Bronchial asthma.** As the result of an inquiry addressed by Heissen, of the Rostock University Medical Clinic, to 137 cases of bronchial asthma, 91 of whom replied, only eight gave a history of familial or hereditary asthma. Heissen concludes that the hereditary factor does not possess the importance attributed to it in the aetiology of asthma, as a hereditary history of asthma in 8·5 per cent. might be found in perfectly healthy families.

Curschmann records cases to show that diseases or functional disturbances of endocrine glands, especially the thyroid, parathyroids, ovaries, very probably the hypophysis, and perhaps the thymus, exercise a distinct causal influence on the origin of bronchial asthma, chiefly by increasing vagotonia.

Cases showing the relation between occupation and bronchial asthma are not common. Rosenbloom records a case of a man, aged 44, who had been a baker for 26 years, and had suffered continually from bronchial asthma for 14 years. Almost every second or fourth week he had an acute attack. Cutaneous tests, with a large number of substances, showed that the only proteins he was sensitive to were rye and wheat and wheat globulin. Rosenbloom quotes Walker, who had found that of 11 patients who became sensitive to proteins after the age of 40, four were bakers and were sensitive to wheat protein, one was an ostler and sensitive to horse dandruff, and one a sifter of green coffee-beans and sensitive to green coffee protein, so that in over half the cases the occupation was responsible for the cause of the asthma.

Peshkin reports a case in a pharmacist, aged 29, of true anaphylactic bronchial asthma, due to inhalation of powdered ipecac, engrafted on a recurrent seasonal bronchitis. There were seven types of food with which positive cutaneous reactions were obtained, though they had no bearing on the existing complaint. After giving up his occupation the patient had only his usual bronchitic symptoms.

F. R. Mason alludes to a doctor who would sneeze when a box of ipecac was opened at the other end of the room, and would have a typical attack of bronchial asthma should he get near enough to this substance.

Ramirez emphasizes the importance of bearing in mind the transmission of anaphylactic or reactive bodies in choosing a donor for blood transfusion. He reports a case of asthma developing two weeks after transfusion of 600 c.c. of blood from a donor who was subject to persistent and long-standing asthma and bronchitis. Both patient and donor gave a positive skin reaction with horse dandruff.

Marfan disputes Landouzy's doctrine that asthma occurs only in tuberculous asthmatic subjects, and maintains that asthma is independent of tuberculosis. In proof of this contention he relates the cases of two asthmatic infants under his care, in whom the cuti-reaction performed three times at intervals of two and three and a half months was always negative. According to Marfan asthma is not very rare in infancy. Its relative frequency at this age is not sufficiently recognized, because it is difficult to distinguish from broncho-pneumonia or recurrent bronchitis. Of 222 cases of asthma observed by Percepied 25 commenced during the first year, 118 between 1 and 10 years, and 79 between 10 and 20 years. Unlike asthma in older children and adults in whom the attack of asthma develops suddenly without being preceded or accompanied by catarrh of the upper respiratory tract or bronchi, in the infant, and up to the age of 5 or 6 years, the asthmatic attack is almost always preceded and accompanied by coryza and bronchitis. The short duration of the attack, its rapid disappearance and recurrence with the same characteristic features, enable it to be differentiated from broncho-pneumonia and expiratory stridor due to tuberculous glands. The prognosis of asthma in infancy is favourable. The earlier the attack is in appearing, the greater are the chances of a permanent cure. On the other hand, if the first attack occurs later, especially after the age of 15, there is a risk of the affection lasting throughout life. Asthma in infants does not leave any sequelae.

Bezançon and De Jong maintain that cytological and chemical examination of the sputum should rank with renal and cardiac examination in the diagnosis of asthmatiform conditions. They consider that cytological, examination of the sputum has almost as much value in the diagnosis of asthma as the investigation of the tubercle bacillus in the diagnosis of tuberculosis. During the last 13 years they have drawn attention to the almost absolute diagnostic value of eosinophilia in the sputum of asthma. They do not attach any importance to Charcot-Leyden crystals, which they found only in exceptional cases, or to Curschmann's spirals. Chemically and microscopically, the sputum in true asthma is free from albumin, which appears only in complicated cases.

In cases of pulmonary sclerosis with chronic bronchitis and emphysema in which attacks of dyspnoea occur, no eosinophils are found if asthma is not the causal condition. But it is especially in men over 50 who present attacks of nocturnal dyspnoea of an asthmatic character that examination of the sputum has considerable value. Some of these cases are examples of true asthma, as is proved by the cytological formula of the sputum. The others are cardio-vascular subjects, and in such cases the formula characteristic of these states is found in their sputum.

In addition to the nine previously reported cases of anaphylactic death in asthmatics, Boughton records a case in which death resulted from an intravenous injection given for desensitization of one minim of horse-serum, which is the smallest amount of serum that has produced death in any reported cases. Both the gross and microscopical appearances of the organs at necropsy showed a striking similarity to lesions previously described in experimental anaphylaxis. As there is an uncertainty in the existing methods of desensitization, Boughton recommends that asthmatics who require curative or prophylactic serums should be tested by the cutaneous method to determine their sensitiveness to horse-serum. If they are not sensitive to horse-serum, therapeutic doses of antitoxin are probably safe. Boughton suggests that antitoxin might be prepared from other animals than the horse for use in patients sensitive to horse-serum.

Lian and Cathala record 21 cases of emphysema subject to frequent spells of bronchitis with paroxysmal nocturnal attacks of dyspnoea, in all of which the oculo-cardiac reflex was more or less markedly positive. The writers conclude that exaggeration of the oculo-cardiac reflex is a very frequent accompaniment of asthmatiform dyspnoea in bronchitic subjects, and probably of essential asthma, and that, therefore, asthma may be regarded as a manifestation of vagotonia. The practical bearing of these observations is that belladonna, which acts by paralysing the peripheral terminations of the vagus, should be given in larger doses in asthma and cases of emphysema with asthmatiform attacks.

Ascoli and Fagiuoli, of the Institute of Medical Pathology of Catania University, report five cases of bronchial asthma successfully treated by irradiation of the hypophysis, a method suggested by the good effect produced by pituitrin in asthmatic attacks. At each sitting three different areas, viz. the frontal and the temporal region on either side were treated. From two to five applications were given in each case.

In children who are old enough F. R. Mason gives benzyl benzoate in capsules containing ℈ij each, four times a day. In the 10 per cent. solution the dose is half a teaspoonful four times a day for a child 6 years old. Increased doses do not seem to be more effective. Benzyl benzoate is best given continuously to patients having frequent attacks, but this is unnecessary when the attacks occur only occasionally.

Woloshin records a case of asthma in a woman, aged 54, in which gratifying results were obtained by hypodermic injection of benzyl benzoate (20 drops every three hours) when oral administration failed to give relief.

**Fibrinous bronchitis.** According to Walker (2), who reports two cases and has collected 31 others from the literature since 1902, the aetiology of fibrinous bronchitis is obscure. He is inclined to regard it as allied to asthmatic bronchitis, bronchiectasis, and chronic bronchitis rather than as a neurosis. Three groups of fibrinous bronchitis may be distinguished, namely, acute bronchitis with expectoration of branching casts, chronic bronchitis with expectoration of branching casts, and cases in which branching casts are not expectorated but are found in the bronchi at autopsy. The usual age of onset is between 30 and 60, with a progressive increase of incidence up to middle life, and then a gradual decline. Occupation, family history, and chemical irritants have little or no bearing on the disease. There is often a history of some acute infectious disease, and almost invariably a past history of chronic bronchitis. In both the acute and chronic forms there are paroxysmal attacks of dyspnoea and some cough, which generally precedes the expectoration of casts. The dyspnoea is chiefly inspiratory in type, the cough is very hard, and there are considerable cyanoses, and frequently a feeling of tightness in the chest. Symptoms are temporarily relieved by expectoration of casts. Haemoptysis is rare. There may be considerable loss of weight and strength. The physical signs are not different from those of ordinary bronchitis, except that when the casts are *in situ* a coarse dry clicking sound may be heard both on inspiration and expiration. There are no definite complications or sequelae, and death is rarely a direct result of the disease.

**Bronchial spirochaetosis.** Farah describes ten cases of bronchial spirochaetosis, observed in Egypt which he treated by intramuscular injections of iodine, the method being based on the fact that fowls which have been given an injection of iodine do not contract *Spirochaetosis gallinarum* when they have been bitten by the argas which propagates the disease. The preparation used by Farah was lipiodol, which contains 54 per cent. of iodine in oil of poppy-seed. A series of 5–10 injections was given, each consisting of 2 c.c. daily, followed by another series of 10–20 injections every two or three days according to the tolerance of the patient.

According to Piñol, of Tortosa, who records an illustrative case, bronchial spirochaetosis is very prevalent in those regions of Spain in which there are plenty of workmen from the south of France, who act as carriers. The diagnosis, which is difficult owing to the resemblance of bronchial spirochaetosis to ordinary respiratory disorders such as influenzal bronchitis, pneumonia, and tuberculosis, can only be established by microscopical examination of the sputum.

In spite of the constitutional disturbance shown by loss of flesh, asthenia, and tachycardia, the prognosis is favourable, provided the disease is recognized and treated in time to prevent it passing into a chronic stage.

Carini reports a case at São Paulo of bronchial spirochaetosis, a disease which had not hitherto been observed in Brazil. As the patient had been in the country a long time, and had almost certainly contracted the disease in Brazil, Carini concludes that bronchial spirochaetosis must exist in that country, and that it is more frequent than is supposed.

V. R. Mason, of the Johns Hopkins Hospital, reports the first case on record of spontaneous infection of the pleural cavity with the *Spirochaeta bronchialis*. The patient, a boy aged 16, after an illness of several months, probably caused by infection of the lungs with spirochaetes, developed an empyema, in the pus of which many actively mobile spirochaetes were found. The prompt and marked improvement following the intravenous injection of neosalvarsan showed that spirochaetes were at least partially responsible for the cause of the disease.

**Non-tuberculous lung infection.** Field, of Iowa City, records eight cases of a disease which has been variously called 'a lobular form of bronchopneumonia of long duration', 'localized bronchitis', and 'subacute and chronic non-tuberculous lung infection'. The onset may occur at any age, but is commonest in children. Females are most frequently affected. The syndrome usually follows acute disease which particularly affects the upper respiratory tract, such as measles, whooping-cough, and influenza, though in some cases it comes on insidiously. Both the onset and exacerbations occur most frequently during the colder months, probably owing to crowding together in ill-ventilated rooms. Adenoids and nasal deformities which cause mouth-breathing are important aetiological factors. Chronic sinusitis is probably present in all the cases. *B. influenzae* is the most frequent predominating organism, but any of the common invaders of the upper respiratory tract may be found, e.g. *Streptococcus pyogenes*, *Staphylococcus albus, Pneumococcus* and *Micrococcus catarrhalis.* The pathological condition probably consists of a localized bronchitis with a lobular distribution, which may clear up or persist in a subacute form, offering a site predisposed to exacerbations and increased tendency to fibrosis. The later changes are bronchiectasis and interstitial pneumonia. Chronic cough, usually most marked in the morning, and expectoration of variable amounts of muco-purulent sputum are the outstanding features in practically all cases. The general health is relatively little affected. Any of the symptoms of tuberculosis, e. g. haemoptysis, moderate fever, or night sweats, may be present. Physical signs are frequently insignificant and occasionally entirely absent. The typical signs are subcrepitant râles, especially after cough, in one of the lower lobes. The percussion note is often somewhat impaired and the breath-sounds somewhat harsh over the affected area. The course of the disease is extremly chronic with a tendency to frequent exacerbations. Some cases recover in from two to six months, but others go on from year to year with only temporary abatement. The prognosis is best in children. The essential treatment is posture, the patient being placed in the Trendelenburg or reversed Trendelenburg position 15 minutes three or four times a day for a long period. Inhalations of tinct. benzoin. co. should be given, and a warmer climate recommended for chronic cases which are refractory to treatment.

Lyter reports eight cases of subacute or chronic non-tuberculous infection of the lungs in which the disease had lasted from three to fourteen years, with an account of the time and character of onset, the physical signs in the lungs, the X-ray findings, the changes in the blood, and examination of the sputum. He considers that the greatest assistance in determining the character of the infection is rendered by a careful examination of the blood. Subacute or chronic pulmonary tuberculosis almost always produces a mild leucopenia with an increase in the percentage of the small lymphocytes, while the non-tuberculous infections in the subacute stage show a rather high leucocyte count in which the polymorphonuclear percentage varies from 78 to 88 per cent., according to the activity of the process. As regards physical signs Lyter maintains that subacute or chronic infection localized in one or both lower lobes should be regarded as non-tuberculous until it is definitely proved otherwise. There is nothing distinctive in the character of the X-ray findings, but the location of the lesion as determined by X-rays is of more value. Nor is there anything in the development or evolution of the general symptoms, taken either singly or collectively, to serve as a differential basis between the two types of infection. On the other hand, the absence of any general or focal reaction after a subcutaneous injection of 2 or 5 mgm. of old tuberculin helps to exclude an active tuberculous lesion.

**Pulmonary abscess.** Several American writers such as Hedblom, Peters, Tewksbury, and Wessler emphasize the fact that pulmonary abscess is a common disease, though until recently it was regarded as rare. Many of the cases after they have passed the acute stage are diagnosed as tuberculosis, and drift into tuberculosis sanatoria and hospitals. Tewksbury, superintendent of the Tuberculosis Hospital of the district of Columbia, states that he has seen 27 cases of non-tuberculous pulmonary abscess during the last three years.

Pulmonary abscess may follow pneumonia, lobar or lobular, or result from aspiration of foreign bodies into the lungs, such as bits of carious teeth, small dental instruments, and pieces of chewing-tobacco. The frequency of pulmonary abscess as a sequel to operations on the upper respiratory tract, especially tonsillectomy, is drawn attention to by Lord, Peters, Clendening, Tewksbury, and Wessler and Schwarz. In a series of 100 cases of pulmonary abscess Lord states that in 25 the disease was due to operations of this kind. Clendening offers the following explanations of the frequency of pulmonary abscess as a sequel of tonsillectomy: (1) The abscess is due in some cases to inspiration of infected material. (2) Motor-driven anaesthesia apparatus, by creating a positive pressure in the pharynx, may operate as a cause. (3) In some instances the abscess is due to metastatic infection through the lymphatics. (4) Swabbing or tampering with the throat after enucleation is the cause of one group of cases.

Tewksbury found that acute pulmonary abscess occurred most frequently in the right lung, 11 out of 14 cases being in the right and only three in the left. The exact situation of the lesion, according to Wessler and Schwarz, varies with the aetiology. In post-operative abscesses and in the aspiration type of post-pneumonic abscess the disease is usually situated in the upper lobes. On the other hand, abscesses due to the aspiration of foreign bodies and the chronic broncho-pneumonic type of bronchiectasis are usually found in the lower lobes.

According to Lord, there are five cardinal signs of pulmonary abscess: (1) foul sputum and foul breath; (2) cough and explosive expectoration; (3) elastic tissue with alveolar arrangement in the sputum; (4) dullness on percussion over a circumscribed area; (5) demonstration by X-ray examination of a cavity with fluid level.

Chalier, of Lyons, describes a cachectic or pseudo-tuberculous form of pulmonary abscess, in which, although the fever may not be very high, a progressive loss of flesh occurs with profound asthenia, reducing the patient at the end of a month to a condition of extreme cachexia.

Perrin-Maréchal has collected 16 cases, including two not hitherto published, of pulmonary abscess due to the pneumo-bacillus. As a rule, the abscess in such cases is single, its size varying from that of a walnut to that of a fist.

Butler describes the subsequent history of the case reported by Erdman and Ostendorf of hypertrophic pulmonary osteoarthropathy following lung abscess (vide *Medical Science*, 1920, **1**, 463), and states that considerable improvement took place in the osteoarthropathy and mental condition after elimination of the focus of infection in the lung.

According to Wessler and Schwarz, the prognosis is bad in the post-pneumonic cases, and in few of these is recovery spontaneous, whereas from an experience of more than 30 post-operative cases in children and adults they found that in about a third recovery took place spontaneously about two months after the onset.

Tewksbury states that the proportion of cures of pulmonary abscess with medical treatment is less than 10 per cent., while with surgical treatment it is from 50–60 per cent. In Lord's series, of 62 operated cases, 35 died in hospital or after discharge—a mortality of 56 per cent.—and of 38 unoperated cases 24 died—a mortality of 63 per cent.—and 14 were alive or could not be traced. Lord considers that delay is justified if the disease has lasted only a short time, if the sputum is purulent, not foul, and does not contain abundant elastic tissue, and if symptoms of sepsis are only slight. Operation, however, in such cases should be considered if recovery or marked improvement does not take place in three or four weeks. Operation is also indicated without regard to the previous duration of the diseases in cases of foul sputum containing abundance of elastic tissue, accompanied by pronounced symptoms of sepsis. Multiple areas are not necessarily a contra-indication, but greatly increase the risk. Cases with diffuse broncho-pulmonary infection, multiple losses of pulmonary substance, and probable bronchiectasis should be excluded as unfavourable. (For the surgical treatment of pulmonary abscess vide *Medical Science*, 1920, **1**, 602–9.)

**Gangrene of lung.** Plaut maintains that only those forms of pulmonary gangrene should be treated with salvarsan, in which the fuso-spirillar symbiosis or the fusiform bacilli and spirilla separately are found in the sputum. If such cases do not quickly improve after injection of salvarsan, the suspicion should arise that a foreign body keeps up the symbiosis, in which case surgical treatment is at once required. Plaut suggests that in cases in which salvarsan has proved effective, without the fusiform bacilli and spirilla having been found, the sputum has not been properly examined.

Alsberg points out that though a rapid cure of pulmonary abscess and gangrene can doubtless be attributed to the employment of neosalvarsan, the fact remains that these conditions may also clear up spontaneously and that neosalvarsan is not always efficacious. He records four cases of pulmonary gangrene, of which two recovered spontaneously and one recovered after neosalvarsan, while the fourth did not clear up spontaneously or react to neosalvarsan, but required operation.

Weiss records four cases of pulmonary gangrene in which salvarsan treatment was quite ineffective. While not wishing to draw conclusions from so small a number of cases, he recommends that when a definite diagnosis has been made too much time should not be spent on salvarsan treatment, as the best chances of a cure consist in an operation by a skilful surgeon after careful clinical and roentgenological localization of the disease.

Several French writers, such as Dufour, Semelaigne and Ravina, Rathery and Bordet, and Houzel and Sevestre, report cases of pulmonary gangrene cured by injections of antigangrene serum composed of a mixture of antiperfringens, antivibrion septique, anti-oedematiens, and antihistolytica serums. The serum in all the cases was given intravenously, and in Bordet and Rathery's case intramuscularly and intratracheally as well.

Loiseleur records a case of pulmonary gangrene in a woman aged 27, cured by artificial pneumothorax, as recommended by Émile-Weil (vide *Medical Science*, 1920, **1**, 468).

**Pulmonary streptothricosis.** According to Zenoni and Macchi, out of a total of 8,399 autopsies performed at the Ospedale Maggiore, Milan, from 1907–20, there were only four cases of pulmonary streptothricosis—in patients aged 9, 18, 56, and 68 respectively. The duration of the disease varied within fairly wide limits, being ten days in the first case, five months in the second, one year in the third, and fifteen days in the fourth. The respiratory symptoms consisted in the first case of pseudo-lobar broncho-pneumonia, with subpleural abscesses and left empyema; in the second case of pleurisy with effusion and purulent bronchitis, preceded by evidence of thickened pleura and abscesses and fistulae in the chest wall. In the third case abscesses also developed in the chest wall and a sacculated empyema developed accompanied by adhesive pericarditis. In three of the cases the streptothrix was associated with other organisms, viz. the tubercle bacillus in one case and cocci in two cases, while in the fourth case the streptothrix was present in pure culture.

Bridge observed some fifteen cases of pulmonary streptothricosis in Los Angeles, California, in the course of a few years, beginning in 1907. Some of the cases resembled tuberculosis in symptoms and signs, and others were mixed cases of tuberculosis and this disease, the two organisms being found in the same sputum. In most cases haemorrhage, usually slight in amount, occurred at some time, but in a few instances large quantities of foetid bloody muco-pus were coughed up almost daily for weeks, the evidence of cavity-formation being present. When blood appeared unmixed with much serum and mucus it usually coagulated firmly and quickly. The cases originated in many different localities, and it was impossible to say that any of them, with one possible exception, arose from a known case of the disease in man or animal. In the pure cases there was no tendency for the disease to begin in the apex of the lung, as is the rule in tuberculosis. The fever in these cases was rarely high, and emaciation was not rapid. The cases of mixed infection sooner or later all died, nor did they show any tendency to improve even temporarily. In no case was the lung lesion secondary to disease in other parts of the body, but in one case there was a skin lesion following that in the lung.

**Pulmonary aspergillosis.** Galdi, of the Cagliari University Institute of Clinical Medicine and Pathology, reports a case of primary aspergillosis of the lung in a girl aged 6, which differed from other cases on record in the source of infection, the child having probably contracted the disease from her habit of cramming sawdust into her mouth. The symptoms were constant cough with profuse sputum, cultivation of which showed colonies of *Aspergillus fumigatus.* There was no constitutional disturbance. The physical signs indicated cavitation of the left lung. The absence of constitutional disturbance was due to the thickness of the sclerotic barrier surrounding the pulmonary cavities.

**New growths of lung.** Cottin, Cramer, and Saloz discuss the diagnosis of primary cancer of the lung in a paper based on the study of 29 cases which had been treated at the cantonal hospital at Geneva during the last 20 years. In only six cases was the condition recognized during the lifetime of the patients, all of whom showed a combination of symptoms whereby the diagnosis could be easily established, viz. insidious onset, pulmonary induration, dyspnoea, cough, continuous haemorrhagic expectoration, enlarged glands, and pain in the chest. The cases in which a wrong diagnosis was made were divided into two groups. In the first the condition was mistaken for a thoracic affection, such as mediastinal tumour, bronchopneumonia, gangrene of the lung, tuberculosis, pulmonary hydatid or empyema. In the second group the pulmonary tumour was latent, being masked by extrathoracic metastases in the liver, brain, and spinal cord.

Renaud records a case of atypical primary epithelioma of the lung, in a man aged 21, remarkable for its rapid course and absence of any characteristic symptoms. Sudden compression of the superior vena cava developed a few days before death, giving rise to oedema of the face and shoulders, cyanosis, dilatation of the veins of the neck, and finally asphyxia.

According to Wildhagen, of Christiania, who reports a case of primary round-celled sarcoma of the right lung in a woman aged 77, primary malignant tumours of the lungs are nearly always carcinomata. Primary sarcomata of the lung are very rare. Boschowsky, who collected 64 cases, states that they are most frequently found in men, and that the right lung is somewhat more frequently attacked than the left. Metastases occur in three-quarters of all the cases. Microscopically, round-celled sarcoma is most frequently met with. Hampeln describes three forms of malignant tumours of the lungs, viz. a bronchial, a pleural, and a lobar form. The bronchial form has a relatively slow course, but the latent stage is absent, and the changes in the large bronchi rapidly give rise to signs of irritation. In the pleural form the disease is situated in the lungs, but the pleural effusion dominates the clinical picture. In the lobar form there may be a latent period of several months to a year. In some cases the disease may run its course without any symptoms. Tumours in the lower lobe are particularly difficult to diagnose, and the course of the disease in such cases is usually rapid.

Carisi reports a case of primary sarcoma of the right lung in a man aged 21, which proved fatal in about four months. The middle and lower lobes were invaded by a tumour the size of a foetal head, which, on histological examination, proved to be a round-celled sarcoma with a predominance of lymphoid cells.

Glass relates a fatal case of mixed-celled sarcoma of the lung with numerous giant cells, in a man aged 51, in whom the condition was at first mistaken for influenzal pneumonia, and then for empyema, before the correct diagnosis of tumour was made.

**Mediastinal pleurisy.** Rehberg, of Tilsit, who records two cases, suggests that, owing to its mild course and the transient character of the symptoms, serous mediastinal pleurisy is probably more frequent than the small number of cases on record would indicate. Three forms of mediastinal pleurisy have been described, namely, dry, serous, and purulent. Dry mediastinal pleurisy was found *post mortem* in Velimirowitsch's case. According to Choyeau, the diagnosis may be made during life by the presence of a rhythmical rub in the cardiac region, at first suggestive of pericarditis, accompanied by fever, general disturbance, and pain in the chest. The condition is distinguished from pericarditis by the greater severity of the pain and the superficial and variable character of the rub, which occurs most frequently in systole and more rarely in diastole. It is also dependent on respiratory movements, ceasing on inspiration and reappearing on expiration. Recovery takes place in a few days, or there is a transition to the serous form. In this variety of mediastinal pleurisy the anterior mediastinum is most frequently affected, but only a few cases have been described by Grancher and Velimirowitsch in children. Serous pleurisy of the posterior mediastinum is shown by an area of dullness near the vertebral column associated with weakened breath sounds, aegophony. and increased pectoral fremitus. Empyema of the mediastinum has often been described. Of 14 cases collected by Savy 8 died and 6 recovered, 2 by spontaneous perforation, 1 by thoracentesis, and 3 by thoracotomy. The anterior mediastinum is most frequently affected.

**Parabronchial pleurisy.** Under the name of 'parabronchial pleurisy' Petzétakis, of Athens, describes a form of pleural effusion which he has found to be very frequent in the course of ordinary acute bronchitis as it was present in 38 out of 51 cases, or in 75 per cent. The effusion has no effect on the general condition, and is manifested by only a few clinical signs. In most cases dullness is absent, while in others there is only a slight impairment of resonance. Less frequently the physical signs are more definite. In such cases there is diminished resonance or even decided dullness with indistinctness of the vesicular murmur. Bronchial breathing and aegophony are exceptional. The effusion is sometimes unilateral, but, as a rule, is bilateral. The naked-eye appearances vary. In the great majority of cases the effusion is serous or sero-fibrinous and perhaps slightly haemorrhagic or turbid. The quantity of fluid in most cases is very small, viz. 1 c.c, 2·5 c.c., and up to 15, 20, or 50 c.c. The cytological formula is as follows: At the onset endothelial cells, isolated or in groups, are very abundant, and there is a variable amount of polymorphonuclears and mononuclears with some red cells. In some cases this formula does not change, or there is a predominance of lymphocytes towards the end, while in others there is a considerable increase in the polymorphonuclears. Cultures and inoculation of the fluid remain negative. The prognosis is excellent, the fluid being readily absorbed, and the general condition not being affected at all. The nature of the effusion is not tuberculous, although it closely resembles a tuberculous sero-fibrinous effusion in its naked-eye appearance. The production of the effusion is to be attributed to toxic irritation and circulatory disturbances due to inflammation of the subjacent bronchial tree.

**Pleuritic hemiplegia.** Hemiplegia in the course of pleural effusion is rare, although numerous articles by French writers have been written on the subject. De Jong and Jaquelin report a case of organic hemiplegia in a man aged 18 occurring four days after an exploratory puncture for a large sero-fibrinous effusion. Tuberculous meningitis could be excluded by lumbar puncture, and the course of the affection was that of embolic hemiplegia. The hemiplegia was probably due to a large effusion compressing the heart and the great vessels, but it was impossible to say whether the embolus had formed in the auricle or in the pulmonary veins.

**Spontaneous pneumothorax.** According to Joerdens, of Dresden, who records an example in a man aged 26, with no history or evidence of tuberculosis and a negative tuberculin reaction, the sudden development of pneumothorax in non-tuberculous and apparently perfectly healthy persons is an infrequent event. Schüle has reported a case of pneumothorax confirmed by autopsy in a typhoid patient following a pulmonary infarct. During the recent influenza epidemic Denecke observed three cases, the first of whom recovered without the formation of an effusion, the second was cured by drainage, and the third, who died shortly after admission to hospital, showed a large pneumothorax due to a necrotic focus in the lung. Joerdens thinks that the most probable explanation of the pneumothorax in his case was the rupture of a subpleural emphysematous vesicle. It is by no means necessary in such cases for there to be a generalized pulmonary emphysema, but isolated vesicles of emphysema due to a previous attack of bronchitis or of whooping-cough in childhood is sufficient to produce the condition.

**New growths of pleura.** According to Du Bray and Rosson primary tumours of the pleura are a very rare occurrence, being considerably less frequent than primary tumours of the lungs or bronchi. The origin of these tumours is obscure, as it is uncertain whether they arise from the lining cells of the pleura or from the intima of the lymphatics. Du Bray and Rosson are in favour of the mesothelial origin, and therefore prefer the term 'mesothelioma' to carcinoma, although most of these tumours have been described under the name of endothelioma. The disease occurs twice as frequently in men as in women, and the greatest number of cases are found between the ages of 30 and 40. It is a little commoner on the right than on the left side, but it may be bilateral. The onset is usually insidious and the course progressive, the average duration of the disease being from six to nine months. Pain in chest, usually of a severe and persistent character, is the earliest and most significant feature. The physical signs are by no means pathognomonic, but a rapidly reaccumulating haemorrhagic pleural effusion is suggestive. The temperature usually remains normal throughout the whole course of the disease; only exceptionally is there a slight evening rise, which is usually due to a superimposed pulmonary infection. The most important and difficult diseases to exclude in the diagnosis are pulmonary tuberculosis with a haemorrhagic effusion and primary malignant disease of the lungs or bronchi.

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## THE CAROTID AND VERTEBRAL ARTERIES: HAEMORRHAGE AND ANEURYSM: CEREBRAL THROMBOSIS AND EMBOLISM.

Two circumstances of late have directed attention to these subjects, gunshot wounds and the operations for the complete removal of the tonsils. Gunshot wounds of the neck, when not immediately fatal, are liable to be complicated by recurrent and secondary haemorrhage from the carotid and vertebral arteries. Aneurysms also form, and, in the course of surgical treatment, thrombosis or embolism may be set up, producing hemiplegia.

The surgeon is of necessity called upon to interfere for haemorrhage and for extending aneurysm, but in presence of a stationary aneurysm an expectant attitude, such as was advocated by Makins from his experience in South Africa, has been confirmed by further experiences during the late war. The lessons derived from gunshot wounds apply to civil practice, in the course of which punctured wounds in the neck by various objects, including fragments of glass, also aneurysms from disease, come under the surgeon's care.

The prevailing opinion of the day requires the complete removal of the tonsils from a vast number of school children, also from recruits for the air service, and other adults. In a good many cases the operation has been followed by haemorrhage, exceptionally by dangerous haemorrhage, and even by hemiplegia.

**The blood-supply to the brain.** The common carotid artery may be compressed or ligatured on one side without any disturbance of the cerebral circulation being noted. It has been known from prehistoric times that the simultaneous compression of both carotids in the neck produces loss of consciousness. The simultaneous ligature of both common carotids is fatal, an interval of three weeks or more should intervene between the two ligations. There are, however, many persons in whom compression of a common carotid on one side causes immediate signs referable to cerebral anaemia. A ligature of the artery on one side may set up an immediate hemiplegia, generally temporary, exceptionally definite and fatal. There are, therefore, patients in whom the anastomosis through the opposite carotids and the two vertebrals is less than the normal. Such deviations from the normal are explained by experiments on animals presenting differences in the arteries supplying the brain.

Astley Cooper ligatured both carotids and both vertebrals at the same time in the dog, after which there was an abundant anastomosis through the deep cervical branches of the subclavian arteries. The rabbit survived the ligature of its truncus brachiocephalicus, but not when its left vertebral was also tied. The horse is quite different; its vertebral arteries tail off to mere threads before reaching the skull, and its basilar artery is supplied from the external carotids, through occipital branches. Hence only one carotid artery of the horse can be ligatured. In the sheep, as illustrated by Chauveau, the internal carotids are absent, their place being taken by branches of the internal maxillary arteries given off from the external carotids. An artery corresponding to the middle meningeal artery of man enters through the foramen spinosum to supply the rete mirabile, and other vessels enter through the foramen ovale and the suprasphenoid canal. In the ox the occipital arteries take part in the formation of the rete mirabile. The ophthalmic artery is one of the terminal branches of the external carotid.

Quain found the internal carotid absent in a man, also the carotid canal, whilst the arterial supply to the brain was reminiscent of the sheep on one side, along with an enlarged internal carotid artery on the opposite side.

Fisher found a complete absence of both internal carotids in a man in whom there had been, during life, no symptoms relating to the abnormality. The vertebrals were enlarged, so that the basilar was nearly double the normal size. Large middle meningeals helped to supply the ophthalmic arteries and an enlarged branch of the ascending pharyngeal penetrated by the foramen vesalii. Experiments by Spencer and Horsley demonstrated on monkeys that the internal carotid is continued directly upwards through the middle cerebral into the lenticulo-striate artery. The immediate effect of closing the common carotid artery is to cut off the flow of blood through the middle cerebral and lenticulo-striate vessels, so that, to prevent anaemia and paralysis of the part of the brain supplied, a re-establishment of the circulation by anastomosis through the circle of Willis is necessary.

When hemiplegia follows immediately upon the ligature of one common carotid, it may be, as in Drüner's case, that the circulation through the opposite carotid is defective. If marked, there is death from general cerebral anaemia. If only a partial failure, the hemiplegia is transient. But the real cause of persistent hemiplegia following upon ligature of the carotid is either thrombosis or embolism. In aseptic cases, clot may be detached from the interior of an aneurysm, or from the distal side of a ligature which has cut through the inner coat. Alternatively a thrombus forms, which, starting at the site of ligation, quickly extends up the internal carotid artery into the skull. In all septic cases the danger from thrombosis and embolism is greatly increased, and the clot starts septic softening of the brain.

**The relation of the tonsil to the blood-vessels.** In order to accommodate their length to all the movements of the neck the internal carotid, also the external carotid and its branches, are extensile. When the head is extended on the neck and turned to the opposite side the arteries are put on the stretch. That is the condition in which they are dissected out by the student, and their position is that which becomes fixed in his memory; they are empty and collapsed. In life, when the head is not extended on the neck, the carotids are rendered slack; they are thrown into curves, and the curves are increased when the full artery is further distended by the cardiac systole.

The **internal carotid** makes an S-shaped curve, a curve outward and backward immediately above its origin, and near the base of the skull a curve inward and forward to enter the carotid canal. This latter curve can be felt from the inside immediately behind the posterior pillar of the fauces, the more plainly when the head is flexed and turned to the same side. When the artery is rather more slack and tortuous than normal, and the wall of the pharynx is thin, this so-called 'pulsatile vessel of the pharynx' is not only palpable but visible. The posterior pillar of the fauces formed by the palato-pharyngeus, joined by the stylopharyngeus, is the land-mark, immediately behind and outside of which, separated only by the thin wall of the pharynx, is the artery.

When the tonsil in enlarging undermines the posterior pillar, it is separated merely by its capsule and the thinned-out superior constrictor from the wall of the internal carotid artery.

The **external carotid** becomes stretched out, when the head is extended, so as to take a straight course. When, however, the head is not so stretched out, the slack artery makes a curve inward towards the wall of the pharynx under cover of the vertical ramus of the mandible. The convexity towards the pharynx is greatest just above the origin of the facial artery, and before the external carotid enters the parotid gland. When the head is not extended, the facial artery has a different course from that with which the surgeon becomes familiar when dissecting out submaxillary glands. When the facial artery is slack immediately after its origin, it makes a curve upward underneath the internal pterygoid to above the level of the styloglossus, where its convexity comes into contact with the superior constrictor of the pharynx immediately outside the lower pole of the tonsil. It gives off its first branch, the ascending palatine, which ascends between the styloglossus and the stylopharyngeus, then between the internal pterygoid and superior constrictor, one branch penetrating the superior constrictor to enter the tonsil, and the other passing over the superior constrictor to the palate. The second branch of the facial at the highest point of its curve, the tonsillar, passes direct into the tonsil, almost horizontally. The elasticity of the tonsillar artery may be regarded as holding the curve of the facial artery almost in apposition with the tonsil. The figure usually given of an almost inch-long artery, ascending to the tonsil, represents the condition found in the dissecting-room. When the tonsil enlarges and undermines the anterior pillar of the fauces it is brought into close apposition with the curve of the facial artery, close to its origin from the external carotid.

In 1811, Alan Burns, in three places noted this close relationship of the tonsil to the adjacent arteries in describing the surgical anatomy of the neck.

**Haemorrhage following acute septic infection.** Acute suppuration may follow upon a primary infection of the fauces, and it may also be set up by infected gunshot and punctured wounds.

(*a*) An acute peritonsillar abscess, when allowed to rupture spontaneously, may be attended by fatal haemorrhage, the wall of the carotid giving way with the release of the contents of the abscess, previously under tension.

(*b*) Haemorrhage, fatal in character, has followed upon puncture of the abscess from within. It is not clear, from many of the cases on record, whether it was the release of tension, as in the previous variety, or whether the knife actually penetrated the artery.

(*c*) When the peritonsillar suppuration extends to the glands of the neck, at first a somewhat circumscribed septic aneurysm may form, then possibly a ligature of the carotid may save life. If the aneurysm has become at all diffused, the ligature cannot be expected to save life. The following cases prove that success is possible.

In Wulff's case a tonsillar abscess in a boy of 8 had set up an aneurysm of the internal carotid. The common carotid artery was ligatured; ten days later the aneurysm suppurated and discharged through the external auditory meatus. The boy recovered.

Ransohoff related how a peritonsillar abscess, after having been opened from the mouth, continued to bleed, so the neck was explored. Among enlarged glands there was found an aneurysm of the internal carotid by erosion of its wall. The common carotid artery was ligatured and healing followed.

Rivers saved his patient by combining ligature with transfusion of blood from the mother. A girl, aged 5, suffering from diphtherial and streptococcal infection of the fauces, developed an abscess, the size of a lemon, in the neck, from which pus containing streptococci was let out. Three days later there was sudden haemorrhage rendering the child pulseless. 300 c.cm. of salt solution was administered subcutaneously, and two hours later 250 c.cm. of citrated blood intravenously. Haemorrhage recurred, the common carotid was ligatured, and the abscess cavity packed, followed by the infusion of 150 c.cm. of citrated blood, and the next day of 200 c.cm. Haemorrhage recurred again when the ligature separated, but proved controllable by pressure, and after a final infusion of 150 c.cm. of citrated blood, and later bilateral middle ear suppuration, the case ended in recovery.

There have been many cases in which the suppuration has first spread to the ear, then through the bone to the carotid canal, when the artery is eroded where it bends from the vertical to the horizontal direction. This complication has been generally fatal. But if, as in the case described by

Spencer, arterial haemorrhage from the ear is at first limited in amount, ligature of the common carotid may prevent a fatal issue.

**Haemorrhage following the removal of tonsils.** Although the danger from haemorrhage after tonsillectomy, arises in only a minute proportion of the innumerable number of cases operated upon, yet the total number of the accidents must be considerable and a few have proved fatal.

The old methods of removal were described by Celsus as follows: 'The tonsillae, called by the Greeks antiades, which have become indurated by inflammation, when within a thin capsule, should be scratched round and evulsed by the finger; but if not separable in this way, they should be hooked up and cut out with a scalpel. The excavation should then be washed out with vinegar and a haemostatic smeared upon the wound.' It was the second method which the surgeons of the eighteenth and nineteenth centuries found liable to be followed by haemorrhage, hence the knife was replaced by the guillotine, which by removing only the projecting part of the tonsil practically avoided the danger from haemorrhage.

The safest, because the most deliberate way of removing the tonsil, is that first mentioned by Celsus, substituting blunt-topped scissors curved on the flat for the finger-nail and finger. The tonsil being held by a hook or volsella, the capsule is snipped round, keeping within both pillars, and then the tonsil is slowly detached by the blunt end of the scissors from within its capsule. But this is voted too slow a procedure; hence after, or indeed without, previously cutting round it, the tonsil is enclosed in a cold wire snare or blunt guillotine, and squeezed out. A tonsil which shells out easily from within its capsule may thus be safely squeezed out. But if it adheres at all to its capsule there is an obvious possibility that portions of the capsule, the superior constrictor, and the blood-vessels outside the latter may be drawn in; operators describe various dragging and twisting manipulations after the blunt guillotine is in position. It is no wonder, when the relation of the tonsil to the arteries is considered, that these combined squeezing, crushing, dragging, and twisting methods of removing the tonsil should be followed by haemorrhage, due to the inclusion of arteries outside the actual tonsil. The danger is the greater if one or other of the pillars is included. In France the piecemeal removal of the tonsil at more than one sitting by means of punch-forceps has been the procedure in vogue. If the posterior pillar is caught in the punch-forceps, a hole may be cut out of the internal carotid artery.

Agnew's case shows the danger of including the posterior pillar in the cold wire snare. Two hours after the operation there was severe haemorrhage which was temporarily arrested by applying adrenalin and compressing the carotid. On the ninth day there was severe secondary haemorrhage, and through a sloughing hole in the posterior pillar was seen the internal carotid, the size of a quill, having a sloughy aspect. The common carotid artery was ligatured; the wound suppurated and healed after two months. At the date of the report the child was in 'splendid health and attending school'.

In Amsden's case it was the anterior pillar which was injured. Secondary haemorrhage occurred through a button-hole in the anterior pillar five days after tonsillectomy. There was considerable shock relieved by subcutanous saline infusion. The hole was sutured and no further haemorrhage occurred.

Sebilleau's paper had the important object of showing how the inclusion of a bit of the posterior pillar in the grip of the punch-forceps had resulted in the additional inclusion of the wall of the internal carotid.

Sebilleau with two others was commissioned to inquire into the death of a patient whilst the operation was being performed. A surgeon, who had previously operated some 500 times upon the tonsils, proceeded to remove the tonsils piecemeal by means of Ruard's forceps from a girl aged 12. The patient was placed under chloride of ether anaesthesia, seated upright in a chair. The right tonsil was first removed by three punches, next the left tonsil in the same way, then adenoid vegetations were scraped away from the back wall of the pharynx by three or four downward strokes of a curette. After this the surgeon saw what he thought was a bit of the upper pole of the right tonsil, and making a rather blind grab at this with the punch-forceps there followed a jet of blood and immediate death. The tonsil in enlarging had extended its base both upward and downward; the upward extension had brought it into contact with the internal carotid wall, out of which a large hole had been punched.

Vandenbosche also recorded a case of instant death whilst the tonsil was being removed piecemeal by Ruard's punch-forceps. A girl aged 18 died in the surgeon's room owing to the internal carotid being perforated. The left posterior pillar of the fauces was found, after death, to have been completely removed in the course of punching away the upper pole of the tonsil, and with the posterior pillar the wall of the carotid had been included. Nevertheless, after making trial of what he calls the American method, he had returned to the use of the punch-forceps. He considered the former method a gross operatic traumatism, risky because producing lacerations in the wall of the tonsillar pouch, leaving a vast bleeding area, long in healing, and ending in a cicatrix liable to produce troublesome constriction of the soft palate and pillars of the fauces. His criticism of the Sluder and allied procedures, as carried out, are not without support in the writings of others.

Labouré's cases relate to injury of the external carotid and its branches outside the anterior pole of the tonsil. In a man aged 22 haemorrhage followed the piecemeal removal of the tonsil by Ruard's forceps, which was not arrested by suture of the pillars; when the external carotid was exposed in the neck it was found that the ascending pharyngeal was the artery wounded, and its ligature arrested the haemorrhage. In a woman aged 25, in whom haemorrhage followed removal of the tonsil by the cold wire snare, bleeding was arrested by tying the external carotid above the origin of its lingual branch. In a man aged 39, after removal by a cold snare, ligature of the external carotid was necessary to arrest the haemorrhage.

The occurrence of hemiplegia after tonsillectomy may be explained by injury sufficient to bruise or rupture the intima without causing a complete perforation. A clot forms and becomes detached as described by Makins and referred to below. Cases have been noted by Scruton and by Gracey. In the latter case tonsillectomy on a girl aged 11 was performed by an assistant, perhaps somewhat unskilfully, under general anaesthesia, after Sluder's method, using a modified Mackenzie guillotine. Left hemiplegia was first noticed by the nurse the next morning, but the patient stated that she found she could not move her arm and leg on recovering consciousness. The hemiplegia began to pass off after three days; she began to walk after 2 months; 6½ months after the operation the leg had entirely recovered, the arm moved slowly with athetosis of the fingers, the angle of the mouth remained paralysed. This condition of the patient was deemed permanent.

In the common practice of combining tonsillectomy with removal of adenoid vegetations, it may be difficult to distinguish the particular manipulation which gives rise to the haemorrhage. In Schmiegelow's case, a boy, aged 12, had adenoid vegetations and enlarged glands in the neck. Without an anaesthetic some scrapes with a Gottstein's curette were made down the middle line of the back of the pharynx; then three or four scrapes on the right side. Severe arterial bleeding was followed by death in a few minutes. The enlarged glands had pressed inwards the right internal carotid, which had been lacerated close to its entrance into the carotid canal.

**Haemorrhage and aneurysm following gunshot injuries.** Gunshot injuries may be distinguished according as the course is practically an aseptic one, even although not absolutely and continuously so.

The expectant attitude adopted and advised by Makins was founded upon his experience in South Africa, where the wounds were caused by the Mauser bullet. Such injuries to the carotid artery were relatively more favourable than those due to bullets and shell fragments in the course of the late war. Further experiences by Makins direct attention to the prevalence of thrombosis and the liability to cerebral embolism, the prognosis being in consequence generally unfavourable. Among 14 cases of gunshot injury of the neck, there were some which presented signs of aneurysmal formation; in others there was an absence of evidence that the wall of the carotid had been perforated, yet there followed thrombosis and cerebral embolism. A lateral injury to the wall of the artery caused rupture of the intima. Upon the rough surface there is produced a clot which adheres to one side only without obstructing the main current. Hence particles from this lateral thrombus are readily detached as the blood-pressure recovers from the shock of the injury. In this way cerebral embolism occurred in cases an hour, or even a day, after the injury.

A case recently published by Drüner illustrates the foregoing description by Makins. An aneurysm the size of a cherry had formed at the inner border of the right sternomastoid muscle and remained unaltered for a month. Then it was exposed and found to be an arteriovenous aneurysm between the common carotid and the internal jugular vein. First the carotid was clamped above and below and 5 c.m. of the internal jugular vein excised. The excision of the aneurysmal sac exposed a hole in the carotid, the size of a millet seed, which was closed by lateral sutures and covered over by a bit of the aneurysmal sac. On releasing the clamps there was a good flow through the artery and the wound was closed without a drain. The operation had been done under a general anaesthetic and three hours later the man had recovered consciousness; he spoke and moved his limbs freely. Six hours after the operation there was paralysis of the left half of the tongue, so that his speech could hardly be understood; this was followed by left hemiplegia, unconsciousness, and death ten hours after the operation, the pulse remaining good to the end. The right carotid had become thrombosed; no sutures had penetrated, but there was a small chink on the inner aspect of the intima, in which the clot adhered and from which the thrombosis had started. The right hemisphere appeared merely softer than the left. Nothing was said as to the state of the opposite carotid or of the vertebral arteries.

Even when the artery is uninjured and the ligation is carried out aseptically, with an aseptic ligature, there is still a danger from thrombosis and embolism as the result of the division by the ligature of the inner coat.

A thrombus forms on the distal side of the ligature which spreads up the artery and from which an embolus may become detached as the anastomosing circulation becomes established. The older the patient, the more likely is this to happen.

The method long ago introduced by Ballance and Edmunds, of applying two compressing ligatures without injuring the intima, is particularly required when ligaturing the carotid in continuity. Yet amongst a large number of papers recently published on the Continent, Perthes seems to be the only writer who mentions a compressing ligature, and he does not refer to Ballance and Edmunds.

The thrombosis and embolism following aseptic ligation may thus start hours or days after the operation; the same is the case after merely a contusion of the intima; besides, clot may at any time after the ligature become detached from the wall of an aneurysm.

By far the larger number of recent communications relating to the carotid have concerned septic injuries. Ligation has had to be undertaken for haemorrhage or diffusing aneurysm, and the results have been determined by the pre-existing injury. Bullets and shell fragments, when not causing fatal haemorrhage, produce contusions and lacerations of the arterial wall, which becomes surrounded by extravasations of blood, and septic necrosis goes on more or less rapidly. The further off from the injury the ligature can be applied on the proximal side of the lesion the better. Therefore there should be no attempt to apply a ligature to the internal carotid, but to the common carotid. Recent experiments by Marquis and Lefeuvre on dogs and rabbits, as well as on the human cadaver, show that after ligature of the common carotid the anastomosing current is from the internal carotid back into the external carotid, and not vice versa. This disproves the suggestion that after such a ligation a current from the external carotid carries clot round into the internal and so to the brain.

Of course sufficient exploration must be made to ensure that the internal carotid is involved, for if it really be the external carotid and its branches which are wounded, to apply a ligature to the common carotid is wrong. One piece of evidence that the complications have not been the fault of the ligatures is that the clot on the proximal side of the ligation, when at a distance from the site of injury, has not suppurated. It may be recalled that there are among the early cases of ligature of the common carotid instances of cerebral softening on *the opposite side* to the ligature, with hemiplegia on *the same side.* This was explained by the statement that the clot on the proximal side of a septic ligature suppurated, and fragments were carried up to the brain by the opposite carotid.

If, then, the common carotid has to be tied, the measures against thrombosis and embolism which are under the control of the surgeon are the application of aseptic ligatures well to the proximal side of the injury and so applying the ligatures as to compress without cutting through the inner coat, at the same time that the septic wound is disturbed as little as possible. Granted the above, then thrombosis and embolism if they supervene can be regarded as the consequences of the injury. The ligature of the common carotid is, for the reasons given above, to be preferred to the more difficult and dangerous ligation of the internal carotid described by Rehn and others.

**The vertebral arteries. Haemorrhage and aneurysm.** Injury to a vertebral artery has been of very rare occurrence, but among the enormous number of gunshot wounds of the neck in the war, a few among the survivors have required surgical interference on account of such haemorrhage or aneurysm. The outcome of recent experience has been similar to that concerning injury to the carotids; an expectant attitude is best, and the safest operation is that of ligature of the first part of the vertebral artery on one or both sides. Where the injury prevents ligature on the first part of the artery of the same side, then the first step should be ligation on the opposite side, to check the circulation distal to the injury. There are several cases on record where the injury had occluded the vertebral artery on the proximal side whilst forcible haemorrhage came from the distal end. The first case by Maisonneuve is an example of the danger of operating at the site of injury. He tied both ends of the divided vertebral artery at the bottom of the wound, but suppuration extended to the spinal canal after the operation, and Maisonneuve exhibited the specimen obtained after death.

The only considerable series of ligations of the vertebral arteries were done by W. Alexander, of Liverpool. He operated under Lister's antiseptic precautions, and among 36 cases were three deaths. His reasons for undertaking the operations were on the theory that epilepsy was set up by an increased vascularity of the medulla, when he might hope, by ligaturing both vertebrals, to prevent epilepsy. He proceeded to divide the clavicular origin of the sternomastoid and to retract inward the sternal head. He next retracted inward the external and internal jugular veins, whilst to the outer side the phrenic nerve was protected. The posterior belly of the omohyoid was cut across, also, when in the way, the inferior thyroid and transversalis cervicis arteries were divided between ligatures. The vertebral artery was exposed between the scalenus anticus and the longus colli muscles, and tied just before its entrance into the foramen of the sixth cervical transverse process. Care was necessary to avoid the field becoming obscured by injury of the vertebral vein as it passed forward.

Alexander's reasons for operating having been proved erroneous, there were subsequently very few occasions for practising his method.

Matas, in 1893, collected 53 cases of vertebral aneurysm; in his case he cut into the aneurysm when he had to plug the artery in the vertebral canal. Fortunately the patient recovered, but it would have been much safer to have begun by tying the first part of the artery.

Küttner, by 1917, had had recent experience over 7 cases of gunshot wounds of the vertebral artery.

*Case I* presented an arteriovenous aneurysm at the root of the neck, on the left side, which showed no improvement after 5 months, yet was not apparently advancing. The aneurysm involved the artery at its entry into the sixth transverse process. The sac being laid open, there was deep haemorrhage controlled by transfixing and ligaturing *en masse.* The rest of the bleeding was arrested by suturing muscle over the sac. The man recovered with permanent paralysis of the vocal cord, and paresis of the sympathetic and of some of the upper fibres of the brachial plexus which prevented elevation of the arm. The alternatives in this case would have been a persistence in an expectant attitude, or the ligature of the first part of the artery proximal to the sac.

*Case II* had a deep-seated arteriovenous aneurysm along with paresis of the left arm, which was not altered by ligation of the superior thyroid, lingual, and facial arteries, but remained stationary whilst under observation.

*Case III* died a week after a gunshot wound involving the right neck and pleura. The bullet had perforated the dome of the pleura, just above which was an aneurysmal sac, the size of an egg, which had followed upon a fracture of the seventh cervical transverse process. The vertebral vein communicated with the aneurysm, but the connexion with the artery was not stated.

*Case IV.* An aneurysm of the left vertebral remained stationary for 5 months, but as the man complained of a continual noise in his head it was exposed. The aneurysm pushed forward the common carotid and may thus have occasioned the noise. The aneurysmal sac extended from the jaw to the clavicle and backward behind the sternomastoid. A finger thrust into the sac touched bare vertebrae. At this point tracheotomy and artificial respiration had to be started, and were kept up until the pulse stopped. The sac was found to reach up to the atlas, it communicated with the vertebral artery between the third and fourth transverse processes, above which the artery was thrombosed up to the basilar. A ligature proximal to the sac would have been a possibly successful expedient.

*Case V.* A gunshot wound of the right neck was followed by haemoptysis and later by secondary haemorrhage which could not be controlled. Hence, on the eighth day, the neck was laid open, decomposing blood-clot turned out, and the vertebral artery found torn across between the comminuted transverse processes of the fourth and fifth vertebrae. The patient died the same night: there was no post-mortem. Here the lesion could be localized by X-ray examination, and a proximal ligature might possibly have saved the man.

*Case VI.* A wound of the right side of the neck had been caused by a fragment of shell which was seen to lie in the right retropharyngeal region. Owing to recurring haemorrhages the wound was explored on the eighth day, when there was bleeding from the vertebral artery at the level of the arch of the atlas, which was controlled by a transfixing ligature. The foreign body had become fixed in the wall of the common carotid artery, and a ligature was placed on that vessel also. The man died the same night. Obviously such cases can be treated by proximal ligation without disturbing the wound.

*Case VII.* A bullet had lodged in front of the body of the first dorsal vertebra. There was a wound of entry the size of a cherry-stone, filled with clot. On proceeding to remove this clot, there was arterial haemorrhage, temporarily controlled by thrusting the finger down the track. The neck was then laid open and the first part of the vertebral tied. The man was progressing well when sent back to a base hospital.

Perthes operated for an arteriovenous aneurysm caused by a shrapnel ball which had lodged behind the second and third transverse processes, because the man complained of giddiness and noise in the head. On cutting into the sac there was severe haemorrhage both arterial and venous. The arterial haemorrhage was controlled by tying the first part of the vertebral artery, the venous haemorrhage by tying the internal jugular vein above and below the communication, whilst that from the vertebral plexus of veins was checked by plugging. The patient recovered; six months later he no longer suffered from noise, but had paralysis of the external branch of the spinal accessory, which had been divided at the operation. At any rate the operator should have begun by the ligature of the first part of the vertebral artery.

Schemmel had operated upon three of the cases noted by Küttner. In a fourth case a fragment of shell had lodged deep between the fourth and fifth transverse processes. On proceeding to remove the foreign body four days after the injury there was severe arterial haemorrhage which came from the distal side, the proximal end of the wounded vertebral being firmly thrombosed. Attempts to secure the bleeding distal end failed and the artery was exposed by a deep dissection and tied on the arch of the atlas, part of which was first removed. The haemorrhage was thus arrested and healing followed. This exposure on the arch of the atlas involves the division of the deep as well as superficial muscles and difficulties due to the large venous plexus. A ligature of the first part of the artery on the opposite side would have been simpler and perhaps as effectual.

Lauenstein's two cases illustrate the one—the importance of the proximal ligature, the other the difficulties connected with exposing the artery on the arch of the atlas. In his first case a bullet had entered behind over the sixth cervical spine and, passing forward, had fractured the right sixth transverse process and then the right mandible, to escape through the parotid gland just in front of the right ear. An aneurysm formed, the size of an apple, and 23 days after the injury the right vertebral was tied close to its origin from the subclavian. After this the aneurysmal sac was laid open and the clot removed. Recovery followed.

In Lauenstein's second case a fragment of shell lodged to the left of the middle line between the atlas and axis. An aneurysm the size of a walnut was taken to be upon the auriculo-temporal artery. Therefore loops to control haemorrhage were first put around the external and internal carotid artery, but when the aneurysmal sac was cut into, the loops failed. Thereupon, the first part of the vertebral artery was tied, but this likewise failed to stop haemorrhage from the sac. After cutting through the splenius and semispinalis capitis muscles the artery could be felt, distal to the aneurysm, pulsating strongly on the arch of the atlas. The artery was ligatured, but free venous haemorrhage continued from the plexus upon which two clamps were left. The ligature on the artery at the atlas gave way 5 days later and the patient died.

Spencer's case was also mistaken for an aneurysm on the external carotid or one of its posterior branches. A bullet had entered behind and below the left mastoid process, and, passing forward, had fractured the left mandible and then escaped by the mouth. Unfortunately, the X-ray examination disclosed only the fracture of the mandible; the bullet had in passing touched the tip of the transverse process of the atlas, causing a horizontal fissure and the wounding of the artery on the inner aspect of the arch. Blood escaping through this fissure outward into the neck caused a diffusing aneurysm although the wound of entry had healed. A ligature upon the external carotid failed to control haemorrhage; the finger thrust into the sac felt blood spurting out through the fissure. A proximal ligature controlled the bleeding so far that a plug could be pushed into the fissure. No further haemorrhage occurred, but the patient did not recover consciousness. He died 8 hours later, probably owing to compression by blood extravasated between the atlas and dura mater around the foramen magnum. The only way in which the patient might have been saved would have been by proximal ligation of the first part of one or both vertebrals. The ligature of the artery on the opposite side would have been the easier; that on the left side would have been somewhat obscured by extravasated blood and swollen lymphatic glands.

Similar lessons are taught by the cases recorded by Joseph and by Schwalbach. Kausch, after describing a failure, also declared in favour of the proximal ligature on one or both sides.

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W. G. S.

## NEUROSYPHILIS

Several observers have remarked on the **increased incidence of neurosyphilis** since the introduction of salvarsan. The relation of neurosyphilis to previous treatment, both arsenical and mercurial, has been investigated by Pette from material at Nonne's clinic, in which sufficient data could be obtained, during the last ten years. This material included 484 cases of tabes and 480 of general paralysis. It was found that about 60 per cent. of these had received no treatment in the early stages of infection and that only about 4 per cent of the tabes cases and 1 per cent. of the general paralytics had been properly treated. From this evidence Pette concludes that efficient mercurial treatment tends to prevent these 'parasyphilitic affections', but not always. As regards the effect of treatment on the incubation period of these affections, he found the longest incubation period (15 years) in those who had received no treatment, and that the incubation period diminished with the intensity of the treatment. Hence it might appear that the effect of treatment was to hasten the development of these affections. Against this it must be noted that the most severe cases received the most treatment. With regard to the influence of salvarsan in this connexion, he found 5 cases of tabes and 9 cases of general paralysis, which had been treated with salvarsan in the primary and secondary stages, in which the incubation periods were from 2 to 6 and 2 to 8 years respectively.

Pette, therefore concludes that insufficient arsenical treatment precipitates 'parasyphilis', but sufficient treatment tends to prevent it.

Concerning cerebrospinal syphilis, he found that it was impossible to decide whether this was more frequent since the introduction of salvarsan, but he was satisfied that it appeared at an earlier date after such treatment. Pette regards a course of weekly doses of 0·45 gm. neosalvarsan, up to a total of 4 gm. as constituting a sufficient course. If treatment is not begun till the secondary stage it is best, in his opinion, to precede arsenical treatment with a course of mercury. Pette concludes that salvarsan properly used is valuable in neurosyphilis, but harmful if given in insufficient quantity. Neuro-recurrences are attributed by him to the same cause, viz. insufficient arsenical treatment.

Lakaye, however, has observed six cases of **neuro-recurrence** after regular and sufficient arsenical treatment in the primary stage. In five of these cases the Wassermann reaction was negative at the time of appearance of symptoms, which suggests that a negative reaction is of little value in prognosis. The amount of arsenobenzol given was from 3·9 to 5·4 gm. in the course of 2½ months. Lakaye thinks that the best preventive of neuro-recurrences is mercury, administered either before, during, or after arsenical treatment. For this purpose he uses 40 per cent. salicylate of mercury injections in weekly doses of 10 cgm. For the treatment of the neuro-recurrence itself, he gives the same and continues the arsenic in small doses gradually increased.

Dreyfus gives the results of ten years' study of the **behaviour of the cerebrospinal fluid** in syphilis. The problems to be solved are: (1) the behaviour of the cerebrospinal fluid in the different stages of syphilis, especially of the nervous system; (2) to what extent these changes affect prognosis and treatment; (3) the effect of treatment on the fluid; (4) the relationship between pathological changes in the fluid and the clinical signs of neurosyphilis; (5) the relative value of the different reactions in the fluid; (6) the times and indications for examination of the fluid; (7) the question whether the condition of the fluid is the decisive factor in prognosis or treatment, or only one of the symptoms.

Dreyfus points out the difficulties of obtaining a series of statistics, owing to the fact that the majority of patients refuse repeated punctures. Hence the conclusions arrived at must depend on as many single examinations as it is possible to collect. This renders the results rather uncertain.

Dreyfus's material comprised 1,067 cases of syphilis at various stages. In these, 3,000 lumbar punctures were performed. A normal cerebrospinal fluid was regarded as one with a pressure of 150–180, a cell count of not more than 5 cells per cubic mm., and negative Wassermann, globulin, and gold tests.

**In primary and secondary syphilis** with no nervous symptoms, pathological changes in the fluid were found in 80 per cent. In the earliest stages these consisted only in increased pressure; in later stages lymphocytosis and increase in albumin; still later, a positive Wassermann reaction. In these cases the pathological changes generally clear up under proper treatment if there are no nervous symptoms. The first course should, however, be followed by a second, third, and fourth, with intervals of six weeks, in order to prevent relapses in the fluid. If the latter is normal 8 to 12 months after such treatment, nervous syphilis is improbable.

**In latent syphilis with no nervous symptoms** changes in the fluid were found only in 19 per cent. of the cases. This low percentage, in cases which had been mostly imperfectly treated, shows a tendency to spontaneous cure, which is supported by the clinical evidence. A cerebrospinal fluid which was normal in the latent stage was never found to become pathological in later years. The serum reaction, however, in this group was positive in 65 per cent. Occasionally the blood was negative and the cerebrospinal fluid pathological.

**In early cerebral syphilis** pronounced changes were usually found in the fluid, with a cell count of 100 to 1,000, and positive Wassermann and gold reactions. The blood was often negative with a positive cerebrospinal fluid in cases treated with salvarsan. The cerebrospinal fluid generally improved with the clinical symptoms after the first course of treatment, but usually relapsed long before recurrence of symptoms. It was found that from four to six full courses of salvarsan at intervals of 6 to 8 weeks were necessary to render the fluid persistently negative. If the fluid is normal 9 to 12 months after the fourth course, recurrence is not probable.

**In cerebrospinal syphilis** the cerebrospinal fluid was seldom normal in the case of active disease, and a positive fluid in all cases probably indicates an active process, even when there are no clinical signs. A negative fluid, on the other hand, indicates a healed process. This signifies that all cases with a positive cerebrospinal fluid and a history pointing to cerebrospinal syphilis should be energetically treated, whether clinical symptoms are present or not. Four courses of salvarsan at intervals of not more than three months are generally required to render the fluid negative.

**In tabes** the relationship of the changes in the fluid to the clinical signs is especially complicated. Changes in the fluid were found in 79 per cent. of the cases. The Wassermann reaction in the blood was positive in 84 per cent. of the fluid positive cases and in 30 per cent. of the fluid negative cases; hence Dreyfus regards the Wassermann reaction as of less value in tabes than in any other form of neurosyphilis. Are cases of tabes with a negative fluid stationary or healed as in other forms of cerebrospinal syphilis? Dreyfus thinks that this is not always so, but that such cases form a group by themselves, mono-symptomatic or oligo-symptomatic, and of lower progress. On the other hand, he says that this sometimes occurs in tabes with a positive fluid, so that further research is necessary. He recommends treatment with salvarsan both in cases with positive and with negative fluids. In 14 cases which were under observation for 7 years a negative fluid and arrest of the symptoms were obtained after 1 to 10 courses of treatment. He thinks that tabes with a negative fluid after treatment is less likely to relapse than any other form of cerebrospinal syphilis. Treatment should be continued for several years, long after the fluid has become negative—three courses in the first year and two in subsequent years. Degenerative processes, resulting in ataxia and optic atrophy, &c., are not influenced, but the crises, pains, bladder symptoms, and perforating ulcer may be relieved. Dreyfus makes no mention of intraspinal treatment.

The technique now used by Marinesco is described by Paulian. The serum is taken either from the patient to be treated or from another patient with syphilis, after an intravenous injection of neosalvarsan. The interval between the injection and the taking of serum is from 1 to 24 hours. The serum is kept on ice for 24 hours, decanted, warmed to 56° C. for half an hour. The quantity injected intraspinally is 10 c.cm., and an equal quantity of cerebrospinal fluid is allowed to escape. After injection the patient lies down for 24 hours. When the serum is taken from another patient a second intravenous injection of neosalvarsan is given two or three days after the first intraspinal injection. As a rule a series of six intraspinal injections are given at weekly intervals, followed by a rest of three months. If necessary the course is repeated. General treatment by mercury and iodides is also given. After a course of six injections the cerebrospinal fluid is said to show diminution in lymphocytosis to nearly normal, and the globulin reaction is sometimes reduced to negative; the Wassermann reaction is attenuated, and in many cases becomes negative. Clinical improvement is also noted. In spinal syphilis, according to Marinesco, spasticity is reduced, sphincter troubles improve, pains disappear, and sensory disorders diminish. In tabes, gastric crises disappear, ataxia improves, and muscular atrophy is arrested. In general paralysis psychic troubles and delirium disappear in recent cases, and memory improves.

Intraspinal treatment with salvarsanized serum has been adversely criticized by many observers. Sachs regards this method as unscientific, because it has been shown that the pressure in the cerebral capillaries is higher than that of the cerebrospinal fluid, that this fluid circulates imperfectly, and that there is very little absorption of it by the cortical and spinal cells. Drugs introduced into the subarachnoid space would, therefore, appear to be rapidly absorbed into the venous system. Therefore he argues that direct injection into the venous system is to be preferred, and by this means he claims that as good, if not better, results are obtained. Referring to the relief of pains, crises, and bladder symptoms by intraspinal treatment in cases of tabes, he remarks that the same result can be obtained by almost any other kind of treatment; and in general paralysis the natural remissions of this disease render it difficult to estimate the effect of any treatment.

Dercum believes that the beneficial effects of intraspinal treatment are due solely to spinal drainage, and not to the action of the salvarsanized serum injected. He looks upon the cerebrospinal fluid as having a purely mechanical function—the hydraulic suspension of the brain and cord—and denies that it plays any part in the nutrition of these organs. He states that drugs introduced intraspinally rapidly pass out by the arachnoid villi and lymph spaces into the general circulation and do not penetrate the nervous parenchyma. Dercum has had considerable experience with the Swift-Ellis method of intraspinal medication by salvarsanized serum and can confirm the beneficial results obtained by this method in cerebrospinal syphilis and tabes, and to a lesser extent in general paralysis, but he claims to have obtained equally good results by simple drainage of the cerebrospinal fluid by lumbar puncture performed at the same time as intravenous injection of arsenobenzol. Further, he states that even better results were obtained, in cases of tabes, by drainage only, performed once a week or once a fortnight, the cerebrospinal fluid being allowed to drain till it ceased flowing. He thinks that the reduced pressure resulting from withdrawal of the fluid leads to a relative hyperaemia of the vessels of the cord and brain, and improved nutrition owing to the increased vascularity. The positive pressure in tabes and general paralysis he attributes to obstruction of the arachnoid villi and lymphatics by the inflamed membranes. The present treatment for cerebrospinal syphilis at his clinic consists of intravenous injections of arsenobenzol, mercurial inunctions, and spinal drainage. In support of the view that the nervous parenchyma may be reached b drugs administered intravenously, Dercum quotes the work of Sachs and Benedict, and of Sicard and Bloch, who found an appreciable amount of arsenic in the cerebrospinal fluid after intravenous injections.

Weichbrodt also found considerable quantities of arsenic in the cerebrospinal fluid of general paralytics one hour after intravenous injection of arsenobenzol. In most cases the amount was nearly equal to that in the blood. Hence, he sees no advantage (as far as arsenic is concerned) in intraspinal injections, since as much arsenic reaches the cerebrospinal fluid by intravenous injection.

Keidel and Moore, on the other hand, uphold the therapeutic value of salvarsanized serum. With regard to a statement by Dercum and Sachs that drugs introduced intraspinally pass away rapidly and do not penetrate the nervous tissues, they mention that the appearance of phenolsulphonephthalein in the urine after subdural injection has been shown to be greatly delayed in cases of neurosyphilis; therefore, that it is reasonable to assume that the excretion of spirochaeticidal substances introduced in the same way is also delayed, and that such substances may remain in contact with the diseased meninges for several hours.

With regard to the **mechanism of intraspinal** treatment, Keidel and Moore have investigated Swift's hypothesis that the irritation set up by the intraspinal injection causes increased permeability of the meninges. The method they adopted was as follows: An intraspinal injection of Byrne's mercurialized serum was first given, and, after an interval of 24 hours, this was followed by an intravenous injection of arsphenamin. Mercurialized serum was chosen because of its irritating effect, which is greater than that of normal serum or of salvarsanized serum. The dose was not more than 0·6 mgm. of mercury, larger doses causing severe reactions. The intraspinal injection was given before the intravenous, so that the highest possible concentration of arsenic might be in the blood while the irritation was at its height. In this way a maximum amount of the drug might be expected to enter the nervous tissues. Intraspinal injections were given once a week for six weeks, and each course was followed by a course of mercurial inunction lasting ten to twelve weeks. No general mercurial treatment was given during the course of intraspinal and intravenous injections. It was assumed that if benefit was to be derived from the theoretically increased permeability of the meninges it would be attained by this method, which provided a maximum concentration of arsenic in the blood at the time of maximum irritation. There were also two other factors to be considered; the hyperaemia of the central nervous system and the direct action of the mercurialized serum. The former could not be estimated, and the latter was limited owing to the small doses employed. Clinical results alone were studied, and the arsenic content of the spinal fluid was not determined. Twenty-five cases were treated, comprising tabes dorsalis, general paralysis, tabo-paralysis, and cerebrospinal syphilis. The clinical results were good in about 60 per cent. of the cases, but the serological results were poor. Comparing these results with those obtained by Swift and others by means of salvarsanized serum, Keidel and Moore conclude that the latter gives better results, especially as regards the effect on the cerebrospinal fluid. They therefore consider that the mode of action of intraspinal medication does not depend upon increased permeability of the meninges. They also remark that aseptic meningitis produced by intraspinal injection of irritants may prove harmful rather than beneficial in the treatment of neurosyphilis. They hold that parenchymatous neurosyphilis is practically always associated with syphilis of the meninges; that in a large proportion of cases meningitis is the principal factor, and that in these cases—early tabes and cerebrospinal syphilis—the greatest benefit is derived from intraspinal treatment.

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C. F. M.

# ABSTRACTS

## SURGERY

**Schiassi, B.** La critica clinica del ' Basedow '. [**Graves's disease.**] *Policlin.*, 1920, **27** (Sez. chir.), 126.

It is estimated that the medical treatment of exophthalmic goitre results in cure in 60 per cent. of the cases. Resort to operative measures, when this treatment fails, is contemplated with some reserve in view of the possible occurrence of such accidents as tetany, haemorrhage, and collapse, which are liable to follow the operation. From a study of his own cases Schiassi considers that these accidents may be avoided if suitable precautions are taken; and he recommends that whenever a fair trial of medical treatment is not followed by decided improvement, operation should be considered. The only operation that he regards as satisfactory is partial excision of the gland. He has used the methods of bilateral excision of the cervical sympathetic and ligature of the thyroid artery in several cases, but has found that in nearly half the cases recurrence happened. On the other hand, in thirty-seven cases of partial excision immediate cure resulted in all, and in twenty-eight of these the operation has been performed sufficiently long to justify the inference of a permanent cure. He attributes these good results partly to a careful technique, but attaches particular importance to the choice of suitable cases and the proper preparation and after-treatment of the patients. In selecting cases for operation it is indispensable to ascertain the condition of the myocardium by repeated examinations of the heart. The degree of regularity in the cardiac rhythm and in the tension of the pulse, and the amount of dilatation both of auricles and ventricles are the points to which attention should be chiefly directed. The X-rays afford valuable assistance in determining the character of the dilatation of the heart; if, after the limits of the heart have been marked out, the patient is put to bed for a month and suitable sedatives administered, a second examination will show whether or not any diminution in the size of the heart has occurred. It is characteristic of Graves's disease that the circulatory symptoms are often transitory; should they be found on examination to be permanent this would suggest the presence of myocarditis and operation should not be undertaken. Other contra-indications are serious gastric crises, profuse and protracted diarrhoea, and chronic diffuse oedema. The author also attaches much importance to signs of any considerable degree of paresis of the parasympathetic system: persistent paresis of the ocular muscles (ptosis, strabismus), marked tachycardia persisting during sleep, and general asthenia, uninfluenced by medical treatment. In presence of these symptoms death during or after the operation would be a likely event.

With regard to the preparation of the patient Schiassi considers that rest in bed for eight or ten weeks is indispensable, and that the patient should be isolated in order to ensure perfect physical and mental tranquillity. Small doses of morphia and veronal are to be given every evening, and during the daytime canabis indica, belladonna, and valerian have been found useful. As the time for operation approaches it is desirable to retain an abundance of liquid in the body, and hence the usual purgative on the day preceding operation is omitted, water is given freely by the mouth, and during the last two days also per rectum. For the latter purpose Schiassi uses a saline solution containing small quantities of calcium, potassium and sodium chloride, glucose, and bicarbonate of soda.

Local anaesthesia should be avoided, since it does not preclude the possibility of some mental excitement on the part of the patient. 'Anaesthesia by inhalation of ether by the drop method, induced by one who is thoroughly conversant with this delicate procedure, always constitutes a factor favourable to the success of the operation, whatever has been stated to the contrary': and an injection of morphia is a useful adjuvant. Ample access to the gland is to be provided for, the incision being horizontal, with the patient's neck moderately extended. The muscles of the anterior part of the neck, except the sternomastoid. are then divided, and, the patient's neck being further extended, one lobe of the gland is isolated and so much of the opposite lobe as it may be deemed desirable to remove. As a mininum, an entire lobe should be removed; as a maximum, one entire lobe and a wedge from the opposite lobe. The isolation of the gland, which Schiassi performs with the aid of a small hook-shaped instrument, is to be conducted without laceration of the tissues, and with as little compression and traction as possible, special care being taken to keep within the capsule at its infero-external portion (parathyroid). If the isolation is carefully performed few vessels need tying, and the loss of blood is insignificant.

The post-operative treatment is analogous to the pre-operative, and should provide complete and prolonged isolation and avoidance of emotional disturbance. The action of the heart is mostly found to be upset for the first few days after the operation, and morphia may be given with considerable freedom. Repeated enemas of potassium bromide and of the saline liquid before mentioned are also of value. Finally, it is necessary that the patient be placed for a prolonged period in circumstances in which the recognized determining causes of the disease are absent.

T. W. P. L.

**BERTOLOTTI, M.** Le anomalie congenite del rachide cervicale. [**Congenital anomalies of the cervical spine.**] *Chir. degli organi di mov.*, 1920, **4**, 395.

The author has brought together his observations in a series of eighteen cases of congenital deformity of the cervical spine, which have come under his notice during the last fifteen years. The paper is well illustrated with photographs of the patients and with radiograms, and forms a valuable concontribution to the knowledge of the subject, both from a clinical and a morphological point of view.

The individual anomalies, which, variously grouped, give rise to distinct clinical types, are in the first place separately considered.

**Ankylosis of the atlas with the occipital bone.** The author considers this to be a congenital deformity and not the result of pathological changes, relying on its frequent association with other evidently developmental anomalies, one of the most frequent being spina bifida.

**Deformities of the skull bones.** These frequently accompany atlanto-occipital ankylosis and comprise defects in the basis cranii, asymmetry of the facial bones, and anomalies of the teeth. Asymmetry of the facial bones is almost always associated with brachycephaly due to flattening of the occipital region, and with a peculiar deformity of the floor of the posterior fossa of the skull. In this deformity the posterior part of the basis cranii descends so as to overlap the upper cervical vertebrae, and the occipital condyles, instead of projecting from the under surface of the skull, lie in a deep depression (basilar depression), bounded laterally by the pyramidal portion of the temporal bones and anteriorly by the body of the sphenoid. The mastoid processes are sometimes atrophied or the air-cells abnormally large, and the temporo-maxillary joint is frequently deformed and its movements interfered with.

**Assimilation of the third cervical vertebra and axis.** This anomaly, when total, results in the formation of a single bone compounded of the two vertebrae and possessing the morphological characters of the axis in a rudimentary form. It is often associated with basal segmentation of the odontoid process, which then forms an independent bone. When assimilation is incomplete there is a tendency to partial absorption of the posterior and lateral parts of the third vertebra, which in this case appears as a laterally placed wedge between the second and fourth vertebral centra.

**Transverse segmentation of the vertebral bodies.** This deformity, which is due to the independent development of the two normal centres of ossification, is always associated with other malformations.

**Vertical segmentation of the bodies and arches.** The segmentation affects the arches more frequently than the bodies, and varies from a mere slit to a wide gap (spina bifida occulta). In cases in which the spina bifida is accompanied by mal-development of the centra, the basal depression and hypertrichosis of the nucha are always present. A specially low descent of the hairy scalp therefore becomes a somewhat important indication of deformities of the cervical vertebrae. The hypertrichosis in these cases cannot be regarded as precisely analogous to that occurring in sacral spina bifida, and it is probably mainly due to a low implantation of the scalp consequent on the defective development of the occipital region and the shortness of the neck found in these cases.

**Basal segmentation of the odontoid process.** This is frequently found in association with assimilation of the second and third vertebrae. The independent odontoid may become ankylosed with the anterior arch of the atlas.

**Hemispondylia.** This term is used to indicate the absence of one lateral half of a vertebra. The remaining portion of the bone is often found to be ankylosed to the vertebrae above and below.

**Dorsalization of the lower cervical region.** When the presence of cervical ribs constitutes the sole deformity the supernumerary ribs are usually relatively well-developed structures; if, on the other hand, other serious deformities are present, they are mostly very rudimentary. In themselves they cause no curvature of the spinal column; they may, however, be associated with defective development of the lateral elements of the corresponding vertebra, less often with hypertrophy of those structures, and in such cases spinal curvature will be present.

Although the cases have a close affinity to one another it is convenient to distinguish three clinical types. In the first type the whole cervical spine is imperfectly developed, and there is a tendency to spina bifida and aplasia of the occipital bone; in the second type numerical reduction of the cervical vertebrae is absent, or at least a minor feature only; the atlas is ankylosed to the occipital bone and other anomalies, such as hemispondylia, transverse segmentation of the centra, and synostosis of the arches, are present; the third type includes the slighter deformities, and more especially ankylosis between the atlas and occipital bone as the sole condition present.

**Clinical Type I.** Four main features characterize this type: The absence or extreme reduction in the length of the neck, flattening of the occipital region of the skull associated with descent of the hairy scalp on to the nape of the neck, an alteration in the position of the pectoral girdle relatively to the thorax, and the production of a so-called 'cervical thorax'. The description given of Case I serves to exemplify this type. The head is sunk deeply between the shoulders with a slight persistent inclination to the left side. All movements of the head are greatly restricted, flexion being impossible on account of the close proximity of the chin to the sternum. The cranium is large and markedly brachycephalic. The nasal bones and lower jaw are deviated slightly to the left. The neck is extremely reduced in length, and of great width. The upper part of the thorax is flattened and depressed anteriorly. Owing to the reduction in the length of the neck and the flattening of the occipital region the hairy scalp overlaps the upper boundary of the back. The vertebral borders of the scapulae are widely separated and the lumbar curve much reduced. In this subject the deformity consisted in an aplasic reduction of the whole cervical spine. What is meant by a 'cervical thorax' is well shown in the radiogram of Case II. Owing to the flattening of the upper part of the chest, the upper border of the manubrium comes to occupy a lower position than normal in relation to the dorsal spine, and instead of a single pair of ribs lying above the level of the sternal notch, as in the normal subject, the posterior parts of five or six pairs are visible above that level.

**Clinical Type II.** This type is characterized by torticollis associated with angular deformity of the cervico-dorsal spine, together with more or less pronounced projection of the ribs on one side, and high position of the scapulae. Reduction in the length of the neck is absent or but slightly marked. The patients frequently suffer pain from pressure on the nerve-roots, and this symptom, together with the angular deformity, produces a close resemblance to caries of the spine, for which the condition may be readily mistaken. The symptoms are, morever, progressive in their development, reaching their maximum in the second decennium of life.

**Clinical Type III.** The sole feature of this form is a torticollis of the muscular type. In most cases this is due primarily to ankylosis between the atlas and occipital bone, but in one case the interesting observation was made of the presence of ossification in the deeper ligaments and muscles of the neck. The torticollis itself is evidently dependent upon an abnormal play of the muscles, and in some of the cases presented transitory variations in intensity.

T. W. P. L.

**Razzaboni, G.** Sarcoma primitivo della vena safena interna (trombizzata). [**Primary sarcoma of internal saphenous vein.**] *Arch. ital. di chir.*, 1920, **2**, 483.

The tumour described in this paper occurred in a male, aged 50, who had previously been free from complaints except varicose veins, which were more marked on the left than on the right side. Without obvious cause the patient was suddenly seized with pain involving the whole of the left leg, and accompanied with a certain degree of fever. Subsequently, the whole limb became swollen and oedematous, and a painful, hard cord developed in the line of the internal saphenous vein. This condition persisted for several years without causing any great inconvenience, when a swelling was noticed in the middle third of the thigh in the line of the vein. In the course of three months the tumour had reached the size of an orange. The inguinal glands were somewhat enlarged, but there was no evidence of disease in the thorax and abdomen. The tumour was firm, nodulated, not adherent to the deeper structures or to the skin, which was somewhat thinned over it and purple, and freely movable, especially laterally. The skin of the thigh was marked by a reticulum of distended venules. After excision of the inguinal glands, the tumour was removed, together with an oval portion of overlying skin and an extensive tract of the saphenous vein above and below. Nine months later, small brown spots appeared, first in the skin of the left leg and thigh, then in the abdomen, and finally in all parts of the body; at the same time severe cachexia developed.

Death occurred in the course of a few months, when innumerable melanotic nodules were found in all the viscera.

The tumour, on section, had a pale grey colour, with distinct streaks of brown, and was surrounded by a well-defined capsule, except at a few localized spots. It was continuous, without a definite line of demarcation, into the saphenous vein above and below, which was transformed into a solid mass of tumour substance in which the wall of the vessel was unrecognizable. The skin over the tumour was in no place adherent to the growth. The inguinal glands appeared to be simply swollen, and free from infiltration by new growth. Microscopically, the growth was composed of short spindle cells, in some places containing pigment giving no iron reaction. A few giant cells were present in places, and the tumour substance was intersected by numerous slit-like and tubular blood-spaces, the walls of which were constituted either of the cells of the tumour or of a single layer of endothelial cells. In the capsule definite tracts of smooth muscle-fibres and an abundance of elastic tissue could be recognized. The saphenous vein above and below the tumour was represented by a solid cord of tumour substance resembling that of the main growth. At a greater distance from the tumour it was occupied by a plug of fibrous tissue resulting, probably, from the organization of a thrombus. T. W. P. L.

**Abrahamsen, A.** Köhlers Sygdom med særligt Henblik paa dennes Patogenese. [**Köhler's disease, with special reference to its aetiology.**] *Hosp.-Tid.*, 1921, **64**, 87–94.

Abrahamsen observes that since Köhler demonstrated three cases of a disease of the tarsal scaphoid bone at the German Roentgen Congress in 1908, about 50 such cases have been recorded. Yet its aetiology is still obscure, and it is regarded as being due to either (1) fracture of a healthy bone, (2) fracture of a dystrophic bone, or (3) delayed ossification, i.e. a simple dystrophy. In support of the last hypothesis Abrahamsen records the following case. A lad, aged 7, began to walk badly four weeks before admission to hospital. There was no history of injury, and the only symptom, according to his mother, was 'stiffness' with rapid tiring in his right ankle after walking. He did not complain of pain, his gait was normal, and he looked perfectly well. The shape and position of the right foot were normal, and the movements at every joint were free. There was also no sign of paralysis or local tenderness, but the circumference of the calf of the right foot was 2 cm. less than that of the left. The X-rays showed hardly a sign of ossification in the right scaphoid bone, the contour of which was only just outlined. On the left side the scaphoid was normal. Though in well-defined Köhler's disease the centre of ossification in the scaphoid bone throws an abnormally small and dense shadow, or a series of small shadows with ill-defined margins, this case was taken to be one of Köhler's disease in an early stage. The patient was given half a tablet of dried thyroid extract (15 cgm.) twice a day. He was weighed every week or two, and when, after two and a half months' treatment, he began to lose weight, this treatment was discontinued. The X-rays now revealed the astonishing fact that the centre of ossification had developed much, and measured 7 cm. Its shape was irregular, and the X-ray picture was now perfectly typical of Köhler's disease.

By the detection of Köhler's disease at an earlier stage than has yet been observed, Abrahamsen believes that a valuable clue to its aetiology has been found. When first examined, the patient exhibited only slight muscular atrophy and a disordered gait which developed only after exercise. So far the case was remarkably negative and uninstructive. The X-rays, however, yielded the surprising information that there was practically no ossification proceeding in the scaphoid bone. Yet, normally, ossification begins in the scaphoid at the age of 4. There was no sign of fully-developed Köhler's disease, as shown by a narrow, compressed, dense centre of ossification, but rather an absence of normal ossification. All the same, the condition was interpreted as an early stage of Köhler's disease, and the correctness of this interpretation was confirmed by the skiagram taken a few months later. Abrahamsen's view that the disease is simply a dystrophy is shared by Köhler himself, who has pointed out that it may be bilateral and unassociated with any history of trauma. C. L.

**LUNDSGAARD, K. K. K.** Det universelle Lysbad i Ophthalmologien. [**Universal light baths in ophthalmology.**] *Hosp.-Tid.*, 1920, **63**, 849–60.

Lundsgaard's paper is a sobering corrective to the recent publications lauding universal exposure of the body to light baths as a short cut to recovery from diseases of the eye directly or remotely traceable to tuberculosis. He began universal exposures in scrofulous diseases of the eyes more than six years ago at the Finsen Institute; his interest waned with the meagreness of the results achieved, but was revived by the successes claimed by other workers, and about three years ago he resumed this treatment on more general lines. Altogether about 200 patients were thus treated, some with diseases of the eyes only, others with lupus in addition. The source of light was in most cases the carbon arc lamp, and the duration of the exposures was 15 to 30 minutes at first, and 1½ to 2½ hours at a later stage. He deals with the following diseases:—**Phlyctenular kerato-conjunctivitis**: all the patients (number not stated) had previously been treated with such standard remedies as silver nitrate, &c., and the only alteration in their day's routine was the inclusion of the light baths in the programme. As a rule no effect of this treatment could be noted; in some there was no change, in others there was a relapse, and in those in which recovery was ultimately effected the 'cure' took so long that it could no doubt have been achieved earlier by other methods. There was only one visible result—rapid and vigorous vascularization—but no real improvement. Indeed, relapses of phlyctenules early in the treatment were so common that their provocation by it could not be dismissed as improbable. Possibly the baths set free toxins which gave rise to focal reactions, as seen after an injection of tuberculin. This hypothesis is the more plausible as Lundsgaard has seen phlyctenules develop after the light treatment of lupus even when this disease was so distant from the eyes as to exclude the possibility of direct action of the light on the eyes. **Keratitis**: 31 cases, most, if not all, tuberculous. All were of the nodular, ulcerating type, and none responded to treatment. **Scleritis**: 8 cases, 5 of which were associated with lupus, and were unaffected by treatment. Of the remaining 3 cases, 2 were probably tuberculous, and they reacted satisfactorily. **Diseases of the lachrymal passages**: 68 cases, 66 being associated with lupus. By itself the treatment was ineffective, but after free opening and scraping of tuberculous passages it seemed to hasten recovery. **Chronic iritis and irido-cyclitis**: 10 cases, all with a positive tuberculin and a negative Wassermann reaction. The results were good in 5 cases, and the improvement was so uniform that it was probably the consequence of the treatment. The increased local injection early in the treatment was interpreted as a focal reaction analogous to that of tuberculin. The results were least satisfactory in two old women, whose age probably contributed to the failure of the treatment.

Only in early tuberculous scleritis and irido-cyclitis in young persons does Lundsgaard think that universal light baths are likely to prove beneficial.

C. L.

## NEUROLOGY

**Rothfeld, J., Freund, J., u. Hornowski, J.** Experimentelle Untersuchungen über die Pathogenese der multiplen Sklerose. [**Experimental investigations on the pathogenesis of disseminated sclerosis.**] *Deutsche Ztschr. f. Nervenheilk.*, 1921, **67**, 257.

These observers obtained completely negative results from animal inoculations with cerebrospinal fluid from cases of disseminated sclerosis and subsequent passage of brain tissue and cerebrospinal fluid from these animals through a further series of animals. In many cases no post-mortem changes were found in the nervous system, in others minimal and non-specific changes were observed. Tuberculosis and coccidiosis accounted for the deaths of most of their animals, and they conclude that great caution is needed in accepting conclusions on so complicated a problem as the aetiology of disseminated sclerosis from animal inoculation experiments.

F. M. R. W.

**Shellshear, J. L. The basal arteries of the forebrain and their functional significance.** *J. Anat.*, 1920, **55**, 27.

Following the observations of Duret and of Beevor, it is commonly held that the claustrum and the external capsule receive their blood from those branches of the middle cerebral artery which supply the cortex of the insula, and not from the basal branches of this artery, and further, that there is no communication between the basal branches to the lenticular nucleus and the cortical arterioles supplying the claustrum.

By a modification of Beevor's injection method, Shellshear finds that there is a series of fine arterial vessels, the claustral arteries, which arise lateral to the lateral striate branches of the middle cerebral artery and supply the claustrum and external capsule. They perforate the surface of the brain at the limen insulae lateral to the anterior perforated space, and therefore lie in series with the lateral striate arteries mesially, and the cortical branches to the insula laterally. Like the other basal arteries, they are end-arteries and do not anastomose with the mesial or the lateral members of the series of which they form the middle member. Nevertheless, there is a capillary communication with both sets. Shellshear finds no vessels of the lateral striate group passing to the thalamus, and thinks that the name lenticulo-optic artery should be discarded.

At the anterior perforated spot he finds an average of from 18 to 20 perforations. These are arranged in two rows running laterally posterior to the lateral olfactory stria. The anterior row receives branches of the anterior cerebral artery, the posterior row and a clump of 5 or 6 perforations at its lateral extremity receive branches of the middle cerebral artery. Laterally again to these are the fine perforations which receive the claustral branches of the middle cerebral artery.

The anterior cerebral artery gives off a recurrent branch, which runs back and then laterally to the outer end of the anterior perforated space, which it perforates near the group of lateral striate arteries. Shellshear says that 'It is of interest here to observe the angles at which these vessels come off from the anterior and middle cerebral arteries . . . the larger the vessel entering the substance of the brain, the more acute is the angle it makes against the direction of the current; and to attain this end both sets from the anterior and middle cerebral arteries leave the parent trunk at a considerable distance from the place of entry into the anterior perforated space'. According to Shellshear, John Hunter alone mentions this peculiarity of the cerebral arteries.

Shellshear points out that the distribution of the cerebral arteries is very precise. It is clear from Sachs's observations upon the nuclei of the thalamus that its subdivision into functional nuclei very closely coincides with the areas of blood vascular supply as determined by Beevor and by Shellshear. There is a similar functional relation between the posterior cerebral artery and the visual cortex, while Stopford's observations on the blood-supply of the pons and medulla point in the same direction.

Shellshear suggests that a good experimental test of the function of a given area of brain might be obtained by cutting off the blood-supply to that area, and he concludes that the cerebral arteries are laid down in definite relation to function, and that their distribution follows phylogenetic and ontogenetic laws. He thinks that such a functional arrangement of blood-supply is well adapted to regulate the activities of a particular function.

F. M. R. W.

**Brun, R.** Beiträge zur Klinik und Pathogenese der Lumbago. [**The origin and symptomatology of lumbago.**] *Schweiz. Arch. f. Neurol. u. Psychiat.*, 1920, **7**, 63.

Brun emphasizes that we have little accurate knowledge of the causes or nature of lumbago. At present, and largely on theoretical grounds, three clinical forms are recognized.

(1) **A myogenic form** in which the muscle is regarded as the primary seat of the disease. Rheumatism and trauma are generally regarded as the factors responsible for this form. Workmen who work half-stripped and subsequently become chilled acquire a rheumatic affection which remains latent until some strain to the lumbar muscles unmasks the condition by the sudden appearance of pain. (Primary rheumatic origin of traumatic lumbago.) Another view is that strain may make the lumbar muscles a 'locus minoris resistentiae' upon which a subsequent rheumatic affection fastens. The importance of actual injury to the muscles, such as tearing, bruising, or haemorrhage, as factors in the production of lumbago is generally deprecated.

(2) **Osteo- or arthro-genic forms.** Torsion at the lumbar spinal joints has been suggested as a cause, but is probably exceedingly rare.

(3) **Neurogenic form.** Lumbago has been described as a true neuralgia of the lumbar nerves, as a toxic neuritis, or as due to injury of these nerves.

In the second section of the paper, Brun analyses twelve personally observed chronic cases of lumbago, all of which presented objective physical signs. From the study of these he finds that trivial injuries may give rise to severe lumbar pain ('Lumbalgie') of long duration, and that these cases are more numerous than is commonly believed; that careful clinical examination reveals in the majority of such cases definite objective physical signs in the affected region; these physical signs include unilateral changes in the lumbar and sacral portions of erector spinae—wasting, hardening, tenderness to pressure, changes of electrical excitability such as diminished faradic response and qualitatively altered galvanic response, and in two instances the presence of transverse furrows in the muscle due to localized spasm.

There were also symptoms referable to the lumbar vertebrae, such as tenderness on pressure over the spines, scoliosis convex to the normal side in three out of four observed cases, and also reflex rigidity of the lumbar spine from pain. Finally, nerve-root symptoms were frequently observed; pain and sensory loss in the distribution of the posterior cutaneous branches of the lumbar and sacral nerves and of the ilio-inguinal nerve, and pain along the distribution of the sciatic nerve. The pain and cutaneous hyperaesthesia in the lumbar region he attributes to this nerve irritation.

From these observations he concludes that chronic lumbago is essentially a perineuritis and neuritis of the posterior cutaneous branches of the lumbar nerves, usually of traumatic origin, and but rarely toxi-infective. The sciatic nerve may be secondarily involved. The condition is frequently complicated by neurotic symptoms. F. M. R. W.

**Rixon, C. H. L., and Matthew, D., with a foreword by Col. Sir A. Lisle Webb. Anxiety hysteria.** *H. K. Lewis, London*, 1920.

The need for a short yet comprehensive book on the treatment of the commoner functional nervous disorders is considerable. The output of psychotherapeutic literature is large, but most of it has been concerned with the intensive cultivation of a small field. There is still room for a book which will describe the symptoms, diagnosis, and treatment of these affections and be of use to the general practitioner. The authors have made a praiseworthy attempt to fill this gap so far as concerns the common psychoneuroses of war. Their treatment is simple; it consists solely in the patient recovering a clear memory of the war experiences which he had suppressed. The technique for this has consisted in employing the method of free association. This has been done from two starting-points: (1) The patient is asked to talk freely about the war, and care is taken that he does not shy at difficult places; (2) he is made to focus on the period about the beginning of an amnesia, and this is cleared up in its entirety. For such a technique nothing is wanted on the part of the doctor but time and patience.

The authors say that though what they have written refers mainly to war cases, exactly parallel conditions obtain among civilians, but here unfortunately the book breaks down. It could not be said, for example, that one of the main reasons for the continuation of insomnia among the latter was the fear of nightmare; the simple expedient of asking a civilian to talk freely about his experiences would lead nowhere, and civilian cases have rarely a definite point of amnesia from which associations could be started.

The authors are careful to disown belief in the sexual theories of Freud, though in all other respects they seem to follow his teaching. They and others might remember that Freud's work, as it is known to the profession in this country, was based wholly on pre-war civilian cases, and therefore on material where the self-preservation instinct was untouched. They might consider why it is that the technique, which in his hands was followed by such erroneous conclusions, has in theirs produced such brilliant results. Was it because of their greater skill, or was it perhaps a fact that Freud was dealing with cases which had a sex basis and that they have been dealing with cases which had a fear basis, and that Freud did not describe the fear basis, because in the well-ordered town of Vienna the emotion did not at that time have much opportunity of displaying itself? Freud has not said, though some of his more foolish followers in this country may have, that the war neuroses are always sexual in origin.

The authors are particularly misunderstanding in their discussion of the interpretation of dreams. They say that it is unscientific to tell a patient that such and such are phallic symbols, and they 'repeat their conviction that the interpretation of any dream can be made only by the dreamer'. That is exactly Freud's teaching. Anything else he dubbed 'wild analysis'. The real difficulty about Freud's technique is one that has seemingly given the authors no trouble, viz. how far free association is to be trusted. Once the view is agreed to that whatever comes from free association is valid, and this is the view of Freud and of Drs. Rixon and Matthew, phallic symbolism will be found connected with all sorts of thoughts in every person, healthy or otherwise, if only the associations are pushed far enough.

The chapter on diagnosis should be re-written in collaboration with a neurologist. The difficulty, for example, in diagnosis between hysteria and disseminated sclerosis does not rest on the occasional presence of tremor and stuttering in the former, but on quite other grounds.

The book is worth re-writing. It is couched in clear simple language, and is practical. It should state clearly that the information contained is applicable to war cases only; the attack on Freud should be dropped, for the book depends on Freud; certain authors should be given credit where due, such as Hurst for the idea of the importance of the cure of hysterical manifestations at a single sitting.

T. A. R.

**Henriksen, P. B. Cultivation of nerve tissue. What it has proved with regard to nerve regeneration.** *Act. Chir. Scand.*, 1921, **53**, 265.

Notwithstanding the title of this paper, the observations it records are purely histological, and are regarded by Henriksen as proving that regeneration of peripheral nerve is a function of the neurilemma nuclei and does not depend upon a new growth of the central stump of axis cylinder.

Immediately after nerve section regressive changes appear in the distal part of the central stump (for about 0·5 cm. of its course). The myelin sheath breaks down and the liberated fatty products stain the axis cylinders so that these give a faint reaction to osmic acid staining, before they also break down in their turn. Simultaneously, there is a co-extensive proliferation of neurilemmal nuclei. At the end of each nucleus a cap of cytoplasm appears and grows out into an elongated fibril. In this way, fine nucleated strands of protoplasm develop, and the distal prolongations of the most peripheral of these grow towards the cut end of the nerve along the empty sheath of Schwann, and finally project from the cut surface to form the bulk of the soft scar tissue which unites the cut ends of the nerve. The development of these protoplasmic strands constitutes the first stage in regeneration. The second stage consists in the laying down, within each strand, of the axis cylinder with its medullary sheath. The rudiments of the new nerve fibre grow from the ends of the nuclei and meet similar rudiments growing out from adjacent nuclei. Where they meet and join the nodes of Ranvier are situated. Regeneration in the fully degenerated portion of the nerve below the section proceeds on identical lines, but is much slower and less profuse, since before restoration can take place the re-establishment of nutrition has to occur.

Henriksen discusses the variations in staining reaction seen in new tissue, and the errors of interpretation made, in his opinion, by other observers, including Cajal, who do not take into account that staining reactions are extremely variable and unreliable. He objects that most histological investigations upon regeneration omit to consider the myelin sheath, which is an integral part of the new nerve fibre.

He considers that the absence of degeneration in a nerve fibre, cut off from its cell body and preserved *in vitro* in plasma, indicates that Waller's law is untenable. He appears to have carried out no cultivation experiments himself, and it is probable that most of his conclusions would not be accepted by histologists nor by those engaged in cultivation experiments.

Numerous colour drawings accompany the paper, but their interpretation is extremely difficult.

F. M. R. W.

## PATHOLOGY AND BACTERIOLOGY

**Prausnitz, C.** Bakteriologische Untersuchungen über Schweinrotlauf beim Menschen. [**Bacteriology of swine erysipelas in man.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1921, **85** (Orig.), 362.

After a brief reference to human cases infected with the bacillus of swine erysipelas, *B. erysipelatos suum*, the author gives short details of a girl, aged 10, who suffered from some congenital cardiac defect. She developed fever of a continuous type with an erythema-like rash and joint pains. Endocarditis supervened and she died in six months. No autopsy was permitted. Repeatedly from the blood during life a bacillus was isolated which bore all the characters of the bacillus of swine erysipelas and was agglutinated by homologous serum. Such a serum in large doses had no therapeutic effect. The source of the infection in the patient could not be traced.

W. B.

**Weiss, H.** **The heat resistance of spores, with special reference to the spores of *B. botulinus*.** *J. Infect. Dis.*, 1921, **28**, 71.

This is an investigation of the heat resistance of the spores of *B. botulinus*, and the effects of several variable conditions which are ultimately responsible for their death. The conditions investigated were—the effect of hydrogen- and hydroxyl-ion concentrations on thermal resistance, and the effects of numbers of spores, desiccation, spore age, and the presence of sodium chloride. The author is also studying the intimate nature of the process of killing by heat under different conditions, and the laws governing it.

The medium used for spore-development was a mixture of two parts of finely ground sheep-brain in one part of water. This was sterilized in the autoclave and used without adjustment, its final reaction being neutral. Spores about one month old were used, at four temperatures, 100° C., 105° C., 120° C., 95° C. Under the best conditions for survival the most resistant spores were destroyed within 5 hours at 100° C., within 40 minutes at 150° C., and within 6 minutes at 120° C. Bath temperatures are indicated. The effect of age on thermal death-rate was next investigated. It was found that the oldest moist spore is the most severely injured during heating. Spores one month old were three times as resistant as those five months old. Another test was made combining both the effect of age and the effect of numbers of spores, the temperature of exposure being 100° C. As before, it was found that the younger spore was the more resistant in both suspensions used, 80- and 18-day spores in concentrations of 1,500,000 and 15,000,000 per c.c. of each. With regard to the effect of numbers, it was clear in the case of the younger spores, both from the period of survival and the greater lag in the more dilute emulsion at any one period, that the greater the concentration the greater the resistance. In the case of the 80-day spore, dilution did not have such a pronounced effect. This indicates that as a culture ages there is a general retrogression. The more resistant ones change more rapidly than the others, with a resulting tendency towards stabilization, the ultimate resistance of the individual more nearly approximating the average resistance.

Next, the effect of five different strengths of sodium chloride at five different temperatures was investigated. The hydrogen-ion concentration was kept practically constant. The thermal resistance was lowered, and the rate of lowering increases as the salt concentration increases. To what particular factor or combination of factors the toxicity of sodium chloride is due, the author was unable to conclude. In determining the effect of the H- or OH-ion concentration on the thermal death-rate, the following were used: hydrochloric acid, oxalic acid, tartaric acid, lactic acid, acetic acid, citric acid, and sodium hydroxide. Each was made up in four dilutions, and their effect was determined on measured numbers of the free spore at five different temperatures ranging from 95° C. to 120° C. The hydrogen-ion concentration was determined electrometrically. The hydrogen-ion lowered thermal resistance of the spore. Oxalic acid was the only one in which the negative ion appeared to exert any toxic effect. From the experimental results obtained it appeared that the greatest resistance to killing by heat occurs close to the neutral point, and that as the hydrogen-ion concentration increases it is accompanied by a rapid reduction in that resistance. In addition, the most pronounced change in resistance occurs just beyond the neutral point, and as the hydrogen-ion concentration increases further the decrease in resistance for a similar change in hydrogen-ion concentration becomes less. In other words, the rate of loss of resistance decreases as the hydrogen-ion concentration increases. The hydroxyl-ion has nearly, if not exactly, the same effectiveness as the hydrogen-ion. The hydrogen-ion concentration changes considerably in a medium in which *B. botulinus* is growing, and ultimately stabilizes itself at a point near $P_H$ 7·5.

In applying these results to the practical problems of canning foods, it is necessary to determine the $P_H$ value of the material to be sterilized immediately before exposure. Any delay between the determination and the processing may cause a sufficient change in the $P_H$ value to require a higher temperature or a longer period of exposure. A safety factor must be allowed. The actual time required in applying such a factor becomes rapidly less as the temperature of processing is increased.

W. A. M. S.

**Nevin, Mary. Botulism from cheese.** *J. Infect. Dis.*, 1921, **28**, 226.

The authoress carried out a bacteriological examination of a cheese, the consumption of parts of which had led to three deaths with symptoms analogous to botulism. Emulsions from the cheese were fatal to guinea-pigs, and a culture of *B. botulinus* was successfully isolated. This culture produced typical toxin which caused the classical symptoms of botulism in a kitten, and which was neutralized by botulism antitoxin. The author's statements of the biochemical characters of the bacillus isolated are not in harmony with those of the Anaerobic Committee of the Medical Research Council (*Special Report Series*, No. 39, p. 27), for she states that milk was coagulated in three days, and that galactose, saccharose, inulin, and mannitol were fermented with the production of gas.

W. B.

**Ciani, G.** Cultura degli anaerobi nelle comuni capsule Petri in presenza di aria. [**Cultures of anaërobic germs in ordinary Petri dishes in presence of air.**] *Ann. d'ig.*, 1920, **30**, 274.

Petri dishes, provided with a rim about 1½ cm. high, ordinary test-tubes, and glass flasks of about the capacity of 100 c.cm. are prepared and sterilized as usual. Slightly alkaline glucose agar is poured into every flask in a quantity sufficient to form a layer 6–8 mm. thick, when poured into the Petri dishes; 10–15 c.cm. of the same agar are poured into every test-tube. These, as well as the flasks, are sterilized once more for 30 minutes in an autoclave under a pressure of half an atmosphere. The test-tubes are then transferred to a water-bath kept at 55°–65° C., together with a larger tube containing a 20 per cent. solution of sodium sulphite previously sterilized by boiling. 0·18 c.cm. of this solution for every c.cm. of agar are added to the tubes. After sowing these with anaërobic germs, such as a *B. tetani* or *B. anthracis symptomatici*, their contents are poured into the previously warmed Petri dishes and these carefully moved about so that germs and sodium sulphite become equally distributed. Whilst this first layer of agar and sodium sulphite solidifies at the bottom of the dishes the same quantity of sodium sulphite as above is added to each of the flasks left in the autoclave at a temperature of about 70°–80° C. After careful moving about of the flask to ensure a uniform distribution of the sodium sulphite, their contents are poured in the same dishes over the existing layer of agar. The dishes are covered with freshly sterilized lids and the whole put into an incubating stove. Colonies can be easily recognized between the two layers of agar as early as 24–36 hours afterwards, but their development is much more vigorous after four or five days. To make preparations one must, of course, use a strong platinum loop, by means of which the protective layer of agar is easily pierced and material obtained, the plates being held upside down with their lids half open. According to the author the *B. tetani* cultivated on his sodium sulphite agar appears to acquire an unusual virulence.

C. d. F.

**Blake, F. G.**, and **Trask, J. D.** (1). **Studies on measles. I. Susceptibility of monkeys to the virus of measles.** *J. Exper. M.*, 1921, **33**, 385.

**Blake, F. G.**, and **Trask, J. D.** (2). **Studies on measles. II. Symptomatology and pathology in monkeys experimentally infected.** *J. Exper. M.*, 1921, **33**, 413.

The authors have studied the question of the transmissibility of human measles to monkeys (*Macacus rhesus*). Intratracheal inoculation was performed on seven animals with unfiltered nasopharyngeal washings from seven cases of measles in the pre-eruptive or early eruptive stages of the disease. In five monkeys, after an incubation period of six to ten days, a constant and characteristic group of symptoms appeared closely resembling those witnessed in human beings. These symptoms were: (1) onset with listlessness and drowsiness after an incubation period, during which the animal appears well; (2) catarrhal conjunctivitis; (3) a well-defined and characteristic enanthem usually confined to the labial mucous membrane; (4) an exanthem consisting of discrete red maculopapules constant in character though variable in extent and duration and comparable histologically with the exanthem of measles; (5) leucopenia; (6) complete recovery after an illness of seven to ten days. The same syndrome was also induced in one monkey inoculated on the mucous membrane of the mouth and nose. A like effect was obtained in two monkeys after the intratracheal injection of nasopharyngeal washings which had been filtered through a Berkefeld N filter. A table is given to show that the virus of measles was transmitted from monkey to monkey in six passages. From the fourth passage monkey the disease was transmitted to three out of four monkeys by means of citrated whole blood administrated intravenously. Cultures were sterile. In the second paper the authors describe in greater detail the symptoms and pathology of the experimental disease and the analogy with human measles is emphasized. W. B.

**ZANELLI, P.** Ricerche sull'agglutinazione. Azione della corrente elettrica continua sui sieri agglutinanti. [**Investigations on agglutination. Action of continuous electric current on agglutinating sera.**] *Ann. d'ig.*, 1920, **30**, 405.

Experiments were made with sera agglutinating the *B. typhosus*, *B. paratyphosus* A and B, and the comma bacillus. The sera were introduced into a U-curved tube through which a continuous electric current of 8 volts and 0·0005 ampère was made to pass for two hours. Before the passage of the current the sera were transparent and neutral; at the end of the experiment the cathodal portion of each serum was turbid and alkaline, the anodal portions had passed into a state of gel and its reaction was acid. Both portions had entirely lost the agglutinating power, which could be restored only by mixing them together in equal volumes. C. d. F.

**BREINL, F.** Ueber Paragglutination. [**On paragglutination.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, **31** (Orig.), 1.

In 1909 Kuhn and Woithe recovered a strain of *B. coli* from the stools of a case of chronic dysentery and found that it was agglutinated to titre by dysentery and typhoid sera and to one-third titre by a paratyphoid A serum. A coccus was also isolated, and was found to be agglutinated by a Flexner serum. Both the culture of *B. coli* and the coccus were agglutinated by the patient's serum, and when inoculated into animals caused the production of agglutinins which clumped dysentery bacilli. This was the phenomenon of 'paragglutination', which has subsequently been investigated by Kuhn and various co-workers. Thus, in association with Ebeling, Kuhn stated (1915) that races of *B. coli*, grown on agar prepared with bouillon, on which *B. dysenteriae*, *B. typhosus*, or *B. paratyphosus* had been cultivated, showed agglutination with various immune sera especially in low dilutions. On this 'specific' agar the agglutinative effects of serum were seen even in subcultures. The present author has repeated these observations, and, while confirming the fact that certain races of *B. coli* show receptors homologous with those of atoxic dysenteric strains, especially when recently isolated, he considers that they rapidly lose this property in artificial culture, and that there is no such thing as 'paragglutination' in the sense used by Kuhn and Woithe.
W. B.

**FRANZ, L.** Chemotherapeutische Untersuchungen zur Behandlung der Wunddiphtherie. [**Chemotherapeutic experiments with a view to the treatment of diphtheria of wounds.**] *Med. Klin.*, 1921, **17**, 107.

The author has made a number of chemo-therapeutical tests *in vitro* to determine the bactericidal effect and penetrating power of a large number of dyes and other chemical substances on diphtheria bacilli. For direct bactericidal action he added the chemical substance, in falling dilutions, to cultures of *B. diphtheriae* on ascitic bouillon, subcultures being subsequently made in 2, 9, 24, and 48 hours respectively. The penetrating power was estimated by measuring the depth in millimetres to which the chemical substance had penetrated in plates containing Loeffler's serum. Tables are given illustrating the results of such experiments. From these it is apparent that the most powerful bactericidal remedies are trypaflavin and argoflavin, and especially hydrocuprine derivatives, such as eucupine and vuzine. Thus, in dilutions varying from 1:2,000 to 1:4,000 trypaflavin and argoflavin killed ascitic-bouillon cultures of virulent *B. diphtheriae* in two hours, the same result being achieved with eucupine in a dilution of 1:4,000, and with vuzin in dilutions ranging from 1:16,000 to 1:32,000. The depth of penetration with methylene blue, crystal violet, trypaflavin, optochine, and eucupine was 14, 3, 14, 7, and 7 mm. respectively. W. B.

**Cattoretti, F.** Ricerche ematologiche e serologiche nei tifosi trattati con vaccino eterologo (anti-colerico). [**Haematological and serological investigations on typhoid fever patients treated with a heterologous (anticholera) vaccine.**] *Giorn. d. R. acc. med. di Torino*, 1920, **83**, 13.

Particular attention was paid by the author to the following points: (*a*) Changes in the number of leucocytes and platelets as well as in the haematological formula. (*b*) Behaviour of the haemoculture before and after the treatment. (*c*) Modifications of the agglutinin curves after the treatment. The conclusions reached are summarized by the author thus: The quantitative alterations of the leucocytes consist essentially of an initial leucopenia followed by leucocytosis, but these vary very much in intensity from one case to the other in so far as the most effective results are characterized by more intense and lasting oscillations in the total number of leucocytes and by a particularly noticeable initial diminution in the percentage of the neutrophils. The platelets diminish in number in every case, but their diminution does not appear to be in relation to the curative effect of the treatment. After the vaccination with a heterologous serum, the haemoculture from typhoid fever patients becomes negative only in those cases which appear to be favourably influenced by the treatment. The agglutinating power of the serum is increased in consequence of the heterologous injections, but independently from their curative effect.

C. d. F.

**Lanzilotta, R.** Sull' uso dei raggi ultravioletti nella preparazione dei vaccini. [**On the use of ultra-violet rays in the preparation of vaccines.**] *Ann. d'ig.*, 1920, **30**, 245.

Experiments were made with emulsions of *B. typhosus* and *B. cholerae gallinarum* prepared with sterile physiological solution from agar cultures. After filtration through sterile paper, the emulsions were exposed for 20 minutes to the action of ultra-violet rays and injected into guinea-pigs in the proportion of 1 c.cm. for every injection. This was repeated 3 or 4 times at intervals of 5 days. Various control experiments were at the same time carried out by the author with the object of making sure of the results, which can be summarized as follows: Cultures exposed to the action of ultra-violet rays are rendered innocuous without losing their vaccinating property. One injection of a culture thus treated is sufficient to immunize a guinea-pig. Vaccines obtained as described compare favourably with those prepared by the usual chloroform method. C. d. F.

**Puntoni, V.** Il fumo del tabacco come disinfettante della bocca. [**Tobacco smoke as a disinfectant of the mouth.**] *Ann. d'ig.*, 1920, **30**, 469.

The idea of making fresh investigations on the disinfectant action of tobacco smoke arose during the recent epidemics of influenza and led to the following conclusions: The remarkable disinfectant power which tobacco smoke has *in vitro* does not appear in the oral cavity of smokers, where it seems to exert only a moderate bactericidal action on slightly resistant germs such as the meningococcus and comma bacillus, even after the smoking of very great quantities of tobacco. Resistant germs, such as the *B. typhosus*, do not appear to be killed in the mouths of smokers, and tobacco smoke does not, even when inhaled, exert any bactericidal action itself beyond the limits of the oral cavity. The various qualities of tobacco have about the same disinfectant power, this being in relation to the weight of tobacco used for each experiment. Tobacco smoke, when filtered through compressed cotton wool, loses all its nicotine and tar derivatives, but has still a noticeable disinfectant power. The bactericidal substances contained in the filtered tobacco smoke are soluble in water. One of them distils at 100° C. and was identified as formaldehyde, the other cannot be distilled and consists of pyrrhol. The disinfectant power of tobacco smoke is therefore due to the action of various substances of which it was possible to recognize tar products, nicotine, formaldehyde, and pyrrhol.

C. d. F.

**Hehewerth, F. H.**, and **Kop, W. A.** **The Wassermann test in patients affected with malaria in the tropics.** *J. Hyg.*, 1921, **19**, 277.

This research, which was carried out in the Central Military Medical Laboratory in Java, deals with Wassermann tests on three Europeans and 41 natives who were infected with malaria. The technique employed comprised an alcoholic extract of human heart. The strength of the complement was determined and a complement unit established. Human serum was used in the same amount as the antigen. The actual test was carried out with 1, 2, 4, and 8 times the complement unit. Patients were examined (1) during the fever while plasmodia were in the blood, (2) after one or two weeks of a good quinine-arsenic course, (3) at regular intervals till negative results were obtained. Two complete tests were carried out, one with heated (56° C.) and one with unheated serum.

Of the three Europeans two were suffering from tertian and one from tropical fever. With heated serum all gave negative results, while with unheated serum all gave a + W.R. which became negative in 2, 3, and 8 weeks respectively.

Of the 41 natives, 9 had tertian, 1 had quartan, and 31 had tropical fever. With heated serum 21 were + and 20 were −, while with unheated serum 38 were + and only 3 −.

An elaborate table is presented giving all the data obtained. From it the authors conclude that in many cases malaria infection causes a positive

Wassermann reaction. A positive reaction may persist for 3 to 6 months. As a rule, however, it disappears under quinine treatment.

With unheated serum positive results are almost always obtained both in natives and in Europeans affected with malaria. With unheated serum the Wassermann test gives positive results for longer periods and in stronger degree in natives as compared with Europeans. W. B.

**Mas y Magro, F.** El sindrome hematico de la anafilaxia. [**The blood picture in anaphylaxis.**] *Arch. Cardiol. y Hematol.*, 1920, **1**, 417.

This long and very careful investigation by Mas y Magro follows on many others by continental authors, but is fuller than most. It is based on experimental anaphylaxis, in rabbits, produced by injections of pilocarpine. The latter drug is convenient to use and forms compounds with the albumins of the blood which serve to initiate the process which terminates in anaphylaxis. This process Mas y Magro divides into three parts as follows:

1. Pilocarpine combines with the albumin of the blood.
2. The resulting compound is hydrolysed, resulting in a pilocarpine which is no longer toxic and a heterologous albumin which is the anaphylactic antigen.
3. Proteolysis of this antigen leads to anaphylactic sensitization.

Mas y Magro has also used in the present research egg albumin and the proteins of the tubercle bacillus. His conclusions are as follows (the more important only being summarized):

1. Certain substances conveniently described as parantigens are capable of acting as antigens by virtue of their forming compounds with the albumins of the blood. Of these may be mentioned pilocarpine, iodine, bromine, arsenic, &c.
2. Drug idiosyncrasy is a parantigenic anaphylaxis.
3. Parantigenic and antigenic anaphylaxis are similar processes, but differ in that the former is not characterized by eosinophilia.
4. Eosinophilia expresses the immunity of the organism to the antigen.
5. In the 'biologic complex' termed anaphylaxis there are to be determined two phases (*a*) of sensitization dependent on proteolysis, and (*b*) of anaphylaxis properly so-called or active anaphylaxis. Each of these is divisible into three phases from the haematologic view-point, an initial phase, a period of hypopoiesis and a terminal phase of haemopoietic adaptation.
6. The blood picture differs according to whether the anaphylactic shock is mortal or not.
7. Splenectomy prior to shock diminishes the intensity of the blood reactions.

In general the blood changes described are those mentioned by other writers, but they are dealt with in unexampled detail. G. W.

**Bond, C. J. On auto-haemagglutination.** *Brit. M. J.*, 1920, ii, 925; 973.

Bond's contribution to the physiology and pathology of the blood concerns itself first with the question of the capacity of red cells to form haemagglutinogens. He finds that fresh cells which do not show autoagglutination may nevertheless do so when allowed to remain several days in contact with gelatin saline, normal saline, or filtered serum. Such cells were pipetted off and tested against native serum and agglutination developed. Cold delayed the development of this power.

This reaction was next compared with the agglutination between different blood-groups. This is specific, but the 'induced' auto-agglutination of Bond is non-specific and is produced in sheep's cells by guinea-pig sera and by the sera of sheep which would not react with fresh cells. It is to be noted, however, that red cells which show specific agglutinability (as in the different blood-groups of Moss, &c.) have this specific property enhanced by the ageing process. This may be due to the addition of a non-specific property, but has in any case an important practical bearing. It emphasizes the need for avoidance of old cells in blood transfusions and probably goes far to explain the frequency of mild shock after transfusion of citrated cells as compared with immediate whole blood transfusions. A further difference between the specific and non-specific reactions is shown by saturation tests. When old red cells are agglutinated by native serum until no more can be agglutinated, there remains in the serum the power of inducing agglutination in other cells for which it has specific affinity. Certain other differences between the two are set forth.

Agglutinogens appear to be impossible to obtain by washing red cells even after fragmentation. No agglutinative power is imparted to the saline washes. It is deduced that agglutinogen can only exist in combination with the stroma of red cells. On the other hand, agglutinin which has combined with agglutinogen and so caused agglutination can be washed away and agglutination again brought about by a fresh dose of serum.

Both specific and non-specific agglutinogens are thermostabile.

Agglutinins are found free in the serum but can be removed by filtration through porcelain.

The second part of Bond's paper extends his observations to cases of disease. In 500 cases submitted for Wassermann reaction test the percentage of positives was 46. Of these only 65 per cent. showed no evidence of auto-agglutination. Of the negative cases 91 per cent. were free from auto-agglutination.

In all cases of pneumonia studied there was a 'double plus' reaction present, and this persisted for several weeks, so that Bond is led to speculate as to whether auto-agglutination may not be in some degree a measure of immunity. Generally speaking, the pneumonia results were true also of other septic processes.

Further investigations were made to determine whether blood from any particular part of the body, e. g. a septic focus or tumour might differ from that of the general circulation in auto-haemagglutinability. Such differences were determined and found to depend on increased agglutinin content rather than on development of agglutinogen. But agglutinin is lost when blood transudes into the tissues as in dropsy or in the formation of lymph, &c.

Traces of agglutinins were found at birth, but Bond confirms the findings of Happ to the effect that the actual blood-group of an infant is not finally determinable before the second year.

Bond next considers the question of auto-agglutinins in fresh and unshed blood. His observations lead him to state that coagulation does not alter the composition of the blood so far as agglutinins and agglutinogens are concerned. He concludes by mentioning the very valid consideration that although we describe these reactions in terms of agglutinins, &c., we are still ignorant of the underlying physics or chemistry of the condition, whichever it may be. G. W.

**Gunn, J. A., and Heathcote, R. St. A. Cellular immunity: Observations on natural and acquired immunity to cobra venom.** *Proc. Roy. Soc.*, Ser. B., 1921, **92**, 81.

It has long been known that congenital or natural immunity cannot be adequately explained by the existence of antibodies in the serum, and it has been assumed that there is a cellular (histogenic) as opposed to a humoral immunity. Relatively little work has been done in the study of histogenic immunity, and what has been attempted has been carried out with the aid of red blood corpuscles as the test object. The present authors show that red corpuscles are unsuitable. In their paper they have studied the natural immunity to cobra venom of rabbits and cats, and the acquired immunity of rabbits to the same poison. The relatively high degree of immunity possessed by the cat is not due to the presence of antivenene coursing in the blood-stream. The heart of the cat was perfused with Locke's solution to which, finally, a known quantity of venom was added. It was found that the heart-muscle of this animal is much less susceptible to the action of the poison than that of the rabbit. There is also a qualitative difference with respect to the reaction of the coronary arteries in the two species, for in the cat they are relaxed by venom, whereas in the rabbit they are contracted from the start. Experiments on the intestine by the method of Magnus again showed quantitative and qualitative differences in the cat as compared with the rabbit. Much higher concentrations of venom were found necessary to kill the intestinal preparation of the cat, and the intestinal movements were relaxed. In the rabbit the venom caused arrest in systole. Experiments on the red blood corpuscles revealed the apparently paradoxical result, that although the cat is much more insusceptible to venom than the rabbit, its blood corpuscles are more easily laked by the haemolysin in the venom.

In order to determine whether, in the course of active immunization, a histogenic as well as a humoral immunity ensues, experiments were undertaken on a rabbit which ultimately was able to withstand 10 minimal lethal doses of cobra venom. The heart and intestine having been freed from antivenene by perfusion preparations were tested and compared with similar ones of non-immunized rabbits. The antitoxin-free heart of the actively immunized rabbit was found to be at least three times as insensitive as that of a normal rabbit, although the red blood corpuscles manifested a greater susceptibility to the laking action of the venom. Experiments on the haemagglutinating action of ricin in normal as compared with immunized animals showed an increased susceptibility in the case of the latter. The red corpuscles therefore cannot be utilized as a reliable index for estimating the degree of cellular immunity. The authors consider that the unusual effects in the case of the erythrocytes may be explained as a result of their having lost their nuclei, and being no longer living cells in the ordinary sense of the word cannot respond to the action of repeated doses of venom in the same way as nucleated cells. The duration of the histogenic immunity is to be the subject of a subsequent investigation.

W. B.

**Otsubo, T. On the action of certain salts on phagocytosis and virulence of streptococci.** *J. Infect. Dis.*, 1921, **28**, 18.

Different results having been obtained by investigators studying the action of the same salt on phagocytosis, the author has undertaken a more complete research. The influence of different salts on the phagocytosis of streptococci both inside and outside the animal body were examined. Test-tube experiments were made with normal rabbit serum, and leucocytes of normal guinea-pig, well washed. The experiments *in vivo* were made in the peritoneal cavity of the mouse, guinea-pig, and rabbit. The peritoneal fluid was in all cases examined three hours after the injection of streptococci, for at the end of this time it was found that a sufficient number of polymorphonuclear neutrophils had emigrated into the cavity in experiments on phagocytosis.

Phagocytosis of streptococci in the peritoneal cavity of the mouse is diminished by M/8 solutions of $MgSO_4$, $MgCl_2$, $SrCl_2$, $Na_2CO_3$, $Na_3C_6H_5O_7$, and $CaCl_2$. It was found that KI and KBr inhibit in lesser degree. Higher dilutions of these salts seem to have no stimulating effect on phagocytosis *in vitro* or *in vivo*. As the dilution increases the inhibitory power is lessened. Repeated injections of some of the salt solutions used appear to reduce phagocytosis in the peritoneal cavity, but no stimulating effect was obtained by subcutaneous injection of higher dilutions of the salts in question. The results were the same in normal and immunized guinea-pigs.

Repeated subcutaneous injections of certain salts reduced the alkalinity of the blood, and also the phagocytic power of the peritoneal exudate. Fewer leucocytes appear in the peritoneal cavity three hours after the injection of M/8 solutions of $MgSO_4$, &c., than after the injection of normal salt solution.

When solutions of certain salts are injected together with streptococcus suspension in mice, and the procedure repeated through many successive passages, some salts may have a greater influence on the character of the streptococcus than others. Thus $Na_3C_6H_5O_7$ seemed to favour the development of virulence, to reduce agglutinability and phagocytability as well as the power to elaborate lysin, but it had no special effect on the power to ferment sugars. W. A. M. S.

**Joltrain, E.** Valeur de la réaction de fixation de Bordet dans le diagnostic de la peste. [**The complement fixation test for the diagnosis of plague.**] *Compt. rend. Acad. d. sc.*, 1920, **171**, 413.

By using unheated emulsions of *B. pestis* as an antigen the author obtained positive results in applying the complement fixation test to the blood-serum of patients, in whom a diagnosis of plague was made by other means, (clinical, bacteriological, &c.). The serum of patients suffering from a variety of other diseases failed to deviate complement under the same conditions. He advises the use of this method for a retrospective diagnosis, when one fails to detect *B. pestis* in buboes or when spontaneous agglutination interferes with the agglutination test. J. R. P.

**Murstad, E.** Om Sachs-Georgi's Syphilisreaktion. [**On the Sachs-Georgi syphilis reaction.**] *Med. Rev.*, 1921, **38**,74-80.

At Gade's Institute, Murstad has compared Sachs-Georgi's with Wassermann's reaction. In 284 out of 314 sera, i.e. in 90 per cent., the two reactions coincided with each other. In 13 cases, S.-G. was negative, W. positive. In 8 of these cases there was a history of syphilis, and in the remaining 5 there was no such history. In 17 cases S.-G. was positive, W. negative; in 9 of these cases there was a history of syphilis, and in 8 there was no such history. After noting that these results coincide with those of many other observers, Murstad discusses the view that the S.-G. reaction is positive at an earlier stage, and that it persists longer under specific treatment, than the W. reaction, but he admits that his investigations do not throw light on this point. As guides to treatment he regards the value of the two reactions as approximately equal. In 4 cases of lepra tuberosa and 1 of lepra anaesthetica, both reactions were positive in the former, negative in the latter. At the present stage the S.-G. reaction must be regarded only as a useful supplement to, but not as a substitute for, the W. reaction.

C. L.

**Taniguchi, T. The Sachs-Georgi syphilis reaction and its relation to the Wassermann reaction.** *Brit. J. Exper. Path.*, 1921, **2**, 41.

296 human sera were examined by the 'incubator method' for Sachs and Georgi's reaction and simultaneously for the Wassermann reaction. 270 cases (91·2 per cent.) gave the same result with the two reactions, comprising 104 positives, 164 negatives and 2 suspicious; 26 cases (8·8 per cent.) showed discrepancies. But none of the discrepancies could be regarded as serious, because the largest proportion (12 cases out of 26) occurred in the cases which were suspicious to the Wassermann test but negative to the Sachs-Georgi reaction, due apparently to the lesser delicacy of the latter reaction, owing to the difficulty of detecting slight precipitation. In general, differences were observed only in the case of weak or doubtful reactions. Accordingly, it seemed unlikely that the discrepancies were due to any essential difference in the nature of the two reactions.

When the amount of complement fixed by the standard amount of serum in the Wassermann reaction was compared with the concentration of serum required to cause precipitation there was also seen to be a close parallelism.

The difference in the behaviour of unheated sera in the two reactions did not necessarily exclude the possibility of their being due to the same constituent, as there was evidence that the thermolabile constituent of the serum, which is not a specific constituent in the syphilis reaction, affected differently the result in the two reactions.

The precipitable substance in the Sachs-Georgi reaction consisted mainly of the lipoids contained in the emulsion. P. F.

**Maltaner, F.**, and **Hoppe, Ella. The chemotactic effect of osmosis upon leucocytosis.** *J. Hyg.*, 1921, **19**, 309.

This paper gives the results of a preliminary study of conditions affecting the movement of leucocytes. The authors state that it demonstrates experimental facts which confirm the assumptions that osmotic force present in aqueous solutions and the permeability of leucocytes for water are the factors responsible for the movement of these cells from place to place. The capillary tube technique of Sicherer (1899) was adopted on account of its simplicity and the possibility it gave for studying the physical conditions present. A great variety of substances was used—bacterial toxins, antitoxins, sera, broth media, neutral salts, citric acid, glycerine, alcohol, &c. The purpose of the experiments was to determine the chemotactic properties of the different substances. All, except physiological saline and alcohol, showed strong attraction for leucocytes. Other experiments were carried out to determine the effect of difference of density upon the movement of leucocytes. Two groups of tests were performed, one in which the density was that of a 0·85 per cent. sodium chloride solution at 37·5° C., and the other in which the density was adjusted to that of guinea-pig serum at the same temperature. In neither of the two sets of tests did any leucocytes accumulate in the capillaries, not even when continued for twenty-two and a half hours. ·The work of Buchner (1890) with bacterial protein (which has generally been accepted as demonstrating the chemical nature of the chemotaxis of leucocytes) was repeated. No evidence of chemotaxis was observed, for no leucocytes accumulated in any of the capillaries containing either bacterial protein or isotonic salt solution. As defining the conditions to be observed in a study of the action of soluble substances in solution on the movement of leucocytes the following conception was formulated by the authors:

(1) There is no inherent force in the leucocyte which can cause it to move considerable distances in a short space of time.

(2) The force which produces this motion resides in the solution, and is physical, not chemical, in nature.

(3) In a solution in which the solute is not at concentration equilibrium with its solvent, there exists a force of diffusion both upon the molecules of the solute and solvent.

(4) The movement of leucocytes is from a less dense to a denser solution or from one of lesser to one of greater concentration in an aqueous medium. This motion is due to the force of diffusion of the water molecules moving in a direction opposite to the force upon the molecules of solute.

(5) A leucocyte is a particle of semi-permeable material which has taken up the solvent water in an amount far in excess of its mass as represented by protein. As a consequence it moves by the force of diffusion upon the water molecules and in an opposite direction to that of the direction of action of the diffusing molecules of solute.

A set of four experiments was carried out to confirm the above. The first showed that an artificial leucocyte (consisting of a spherical cell of collodion and filled with water) moves in water toward a source of diffusing saccharose. Another test demonstrated the movement of leucocytes over a considerable distance towards a source of diffusing sodium chloride. The third showed the presence of osmotic force and the effect of the diffusion of sodium chloride on the rate of settling of leucocytes from a suspension. The last test showed that an insoluble substance, like casein, has no effect on the rate of settling of leucocytes from a suspension, but that when a soluble substance is produced by tryptic digestion, the same effect is observed as with sodium chloride.

Hence with the substances used, and in an aqueous medium, leucocytes move in a direction opposite to that in which the dissolved substances are diffusing. This they consider to support the hypothesis that the movement of leucocytes is due to the force of osmosis which exists in a solution not at concentration equilibrium, and that the application of that force depends upon the greater permeability of leucocytes for water than for the dissolved substances. W. A. M. S.

**Dreyer, G. A simple procedure for the accurate enumeration of blood-cells and bacteria without the use of a counting chamber.** *Lancet,* 1921, i, 219.

The method described is founded upon that of A. E. Wright in which the suspension of bacteria to be counted is compared with the number of red corpuscles in human blood. Its advantages, however, are numerous. First, instead of human blood of variable cell content, hen's blood fixed with corrosive sublimate and accurately counted in a haemocytometer chamber is diluted to contain 20,000 cells per c.mm. and is used as the standard. The precise details of fixation should be followed in the original. The author has kept such standard suspensions at room temperature without alteration for eight months. The advantage of hen's blood is that it cannot be confused with that of mammals and thus it can be used for counting human blood corpuscles. To do this, 0·1 c.cm. of human blood is placed in 19·9 c.cm. of 1·3 per cent. solution of corrosive sublimate in saline solution. The mixture is shaken and 0·1 c.cm. is transferred to a small test-tube. The standard suspension of hen's corpuscles is then shaken and a similar quantity (0·1 c.cm.) is transferred to the same test-tube which is agitated so as to mix the two suspensions thoroughly. A drop is then placed on a clean slide and covered with a slip, care being taken to exclude air bubbles. Count with a $\frac{1}{6}''$ objective using a square diaphragm in the ocular. The cells are enumerated in 50 square fields.

$$\frac{\text{No. of non-nucleated cells}}{\text{No. of nucleated cells}} \times 4{,}000{,}000 = \text{No. of red cells per c.mm. of the}$$

blood examined.

For dealing with bacteria the standard is prepared in a slightly different way to contain 30,000 cells per c.mm. The bacterial suspension being diluted 1 : 200, 1 vol. of the standard, 1 vol. of the bacterial dilution and 1 vol. of 0·5 per cent. methylene blue solution are mixed and the bacteria and blood-cells are counted in 80 fields. The results are shown to have a smaller variation from the mean than can be obtained with the finest counting chamber.

P. F.

**Agulhon et de Leobardy, J.** Remarques sur l'emploi en hématologie des colorants complexes basés sur la méthode de Romanowsky. [**On the employment in haematology of complex stains based on the Romanowsky principle.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 120.

It is well known that a very careful adjustment of the degree of alkalinity or acidity is often necessary to bring out optimum staining characteristics. This is especially true of the Romanowsky type of stain. With this in mind the authors have set out to determine what are the corresponding $P_H$ values for optimum effects.

In haematology the water used for purposes of dilution should be at the acid limit of the neutral point of phenol red. The best results are obtained by neutralization in the presence of brom-cresol. Water, which is acid to methyl red will not yield a good coloration with basophilic elements. The optimum $P_H$ is 6 to 7.

In protohistological work one should adjust the water to neutrality with phenol red, or cresol red, and α-naphtholphthalein, or, better still, with neutral red (orange tint). The optimum $P_H$ is 7 to 8. Beyond this, e.g. water neutralized to thymolsulphonephthalein or to phenolphthalein is too alkaline. Practically speaking, ordinary commercial distilled water can be used, without alteration, for work in haematology. One should, however, be cautious in dealing with water which has been for a long time in glass vessels, it tends to become alkaline. If such is the case, it may be corrected by the addition of very dilute acetic acid (a maximum of 1 per cent. when working with a litre of water). Use phenol red as indicator. Old films likewise become more alkaline.

The authors' technique for the rapid Giemsa method is as follows:

First stage: Place on the film a sufficient number of drops of the dye to cover it. Allow it to remain for 30 seconds.

Second stage: Place on it as many drops of distilled water as were taken of dye. Mix, by agitation, and allow to remain for half an hour. The distilled water should be neutral to neutral red if it is to be used in connexion with protozoa. If to be used for blood-films, it must not be alkaline to phenol red.

Third stage: Wash with distilled water, dry with blotting-paper.

W. A. M. S.

**Gram, H. C.** Volume des globules du sang et rapport de ce volume à l'hémoglobine et au nombre des cellules. [**The volume of the red blood corpuscles and the ratio of this volume to the haemoglobin and to the number of cells.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 151.

In order to determine the volume of blood-cells, 0·5 c.cm. of an isotonic solution of sodium citrate (3 per cent.), is mixed with 4·5 c.cm. of venous blood. The mixture is placed in a graduated tube and centrifugalized for 90 minutes at 3,000 revolutions per minute. If the amount of the deposit is $P$ c.cm., and the original volume of blood $S$ c.cm., then the per cent. volume is easily given by the formula $100\,P/S$. With care these results are nearly identical with those given by the haematocrit, the error being only $\frac{1}{2}$ c.cm. per cent. The average value in man varies from 41 to 51 per cent., and in women from 36 to 45 per cent. The ratio between the volume of the cells and their number, forms what the author calls 'a volumetric index', given by the formula Vol. index = vol. $\% \times 0{\cdot}12/G$, where $G$ is the number of cells per c.mm. It is not shown how this formula is arrived at, and, moreover, there seems to be some omission. The following appear to be the steps intended:

$$\text{Vol. index} = \frac{\text{vol. \% of globules}/42}{\text{corps. per c.mm.}/5{\cdot}10^6} = \frac{\text{vol. \%}}{G}\cdot\frac{5}{42}\cdot 10^6$$
$$= \frac{\text{vol. \%} \times 0{\cdot}12}{G} \times 10^6,$$

i.e. the factor $10^6$ is missing.

These volumetric indices correspond closely to the colour indices. The author notes that an average blood-count is more often five and a half millions per c.mm. than the conventional five millions. Obviously the agreement between the colour and volumetric indices is not so good in the case of anaemias, due to the false suppositions made in the calculations. In the case of microcytic anaemia the difference is 0·2, and in pernicious anaemia it is 0·05.

W. A. M. S.

**Westergren, Alf. Studies of the suspension stability of the blood in pulmonary tuberculosis.** *Acta med. scandinavica*, 1921, **4**, 247.

The author seeks to examine the suspension stability of blood corpuscles in cases of pulmonary tuberculosis. A reference is first made to the work of Fåhraeus (1917) in this direction. He first modifies Fåhraeus's method of taking blood by a slight alteration in the make of a 'Record' syringe. The blood taken from a vein in the arm is placed in a series of upright glass tubes 30 cm. long, internal diameter 2·5 mm. The lower end is drawn out to a point, such that the 1 c.c. mark is 200 mm. from the bottom. After an interval the depth of the plasma layer is measured, and observations graphically noted. He has made about 3,000 such examinations on 500 patients. The width of the fluctuation of the phenomenon as shown by 'stability' reaction is considerable. The height of the plasma layer is measured in mm. per hour (at end of 1, 2, and 24 hours). These investigations were made on male patients only (the Stockholm Hospital for tuberculosis at Söderby), the age varying from 15 to 60 years. Repeated examinations were made of any one case, and at different intervals of time. A series of plates are reproduced, divided up according to Turban's classification of the stages of tuberculosis. Sedimentations in mm. per hour are plotted, as are also the corresponding temperatures of the patients (always per rectum).

From an examination of his cases, the author considers that a reaction of the organism to the pathological process, proceeding or just passed off, is expressed in the suspension stability of the blood. The degree to which the suspension stability is reduced, on the whole, corresponds with the extent of activity which the process might be presumed to possess. The stability reaction seems to be a more reliable measure of the tuberculous activity than temperature. Though reduction of the stability is not a specific reaction, the author thinks it may have a diagnostic value for tuberculosis. Prognostic bases might be thus obtained. It is considered that the cause of a reduced 'suspension stability' of the blood is an increase in the fibrinogen (or globulin) content. It appears that in tuberculosis, increases ought to be found in the fibrinogen and globulin content of the plasma. The stability reaction affords the easiest estimation of these increases.

W. A. M. S.

**Price-Jones, C. The diurnal variation in the sizes of red blood-cells.** *J. Path. & Bacteriol.*, 1920, **23**, 371.

This paper is an endeavour to explain the variations in the mean diameter of the red blood-cells in a healthy person. Blood was obtained by pricking the finger or ear, and films made in the usual way. They were dried in air without heat, fixed, and stained in Jenner for two minutes, and afterwards for two minutes in a weak aqueous solution of eosin for intensification. A form of projection apparatus was used to produce magnification and to measure diameters. The cells were classified into groups, progressing by 0·25 $\mu$, and the mean diameter of 500 cells is taken to represent the mean diameter of the red cells for any specimen of blood. On some occasions moist preparations were used. In an experiment to demonstrate the effect of violent exercise on the diameters, both dry and moist specimens were used. In both, the diameters showed an increase of over 0·55 $\mu$, followed by a diminution of about the same amount. Further experiments demonstrated that changes in diameters correspond with changes in volume. Volumes were obtained by centrifuging in calibrated tubes, all the samples being treated simultaneously, and values obtained were relative to the control sample. The methods of statistical practice are used to determine standard deviation, probable error of mean, &c. A graph exhibits the diurnal variation, namely, a gradual increase during the day and a diminution during sleep. This suggests that the red cells swell and shrink in association with bodily activity. Further experiments showed that violent exercise increased these changes, gentle exercise had no special influence, while rest in bed did not abolish these diurnal variations. These facts suggest that the variations in size of the red cells are due to differences in the reaction of the blood. The latter was determined by the method described by Boycott and Chisolm. The red cells swell with an increase in acidity and shrink when the blood is alkaline. The latter experiments were performed *in vitro*. Several simultaneous determinations of blood reaction and red cell diameters were made on the author before and after short violent exercise. In each case an increase in diameter has been associated with a diminution in alkalinity. After forced breathing the mean diameter of the red cells diminished by 0·5$\mu$. As the $CO_2$ re-accumulated, and the alkalinity of the blood returned to normal, there was a rapid restoration to the normal diameter. W. A. M. S.

**Bechhold, W.** Bau der roten Blutkörperchen und Hämolyse. [**Structure of red blood corpuscles and haemolysis.**] *München. med. Wchnschr.*, 1921. **68**, 127.

In this important paper fresh light is thrown on the structure and composition of the cell membrane as exemplified in the stroma of the red blood corpuscle. The paper is a summary of work carried out by the author and numerous collaborators. Their conclusions are based upon consideration of the colloid chemistry of the chemical constituents of the stroma, namely, a protein substance and the lipoids lecithin and cholesterin.

The structure of the stroma has as a framework a delicate elastic network of a protein substance, insoluble in water and in a state of imbibition. This network surrounds the cell as the network of a balloon surrounds the balloon. It does not permeate the cell in the manner of a sponge, as has been supposed by some. This network of protein is 'dressed' with a mixture of lecithin and cholesterin in certain definite proportions, so that the lipoid mixture fills the protein network as a membrane of a soap solution can be made to stretch across the meshes of a wire network.

The lipoid mixture remains attached to the protein network by the force of adsorption. From measurements of the surface tension of lecithin solutions in water and salt solutions in different concentrations, it is concluded that those concentrations which correspond to the physiologically 'normal' solution present the conditions under which the adsorbability of lecithin is most pronounced. This effect is enhanced when physiologically 'balanced' solutions of different salts (such as Ringer's solution) are used.

The lipoid mixture of lecithin and cholesterin has certain other peculiar characteristics. Lecithin in water or salt solution exists partly in the form of a true solution and partly as an emulsion of fine droplets of lecithin in a state of imbibition. Cholesterin is quite insoluble in water or salt solution, but a solution of lecithin in saline has the power to dissolve cholesterin.

When certain definite relative quantities of lecithin and cholesterin are used the result is an optically homogeneous colloidal solution of lecithin and cholesterin. If this salt solution is diluted with water it becomes 'demixed': it ceases to be optically homogeneous and brilliant droplets of cholesterin become visible in dark ground illumination.

These properties of the membrane determine the conditions under which haemolysis occurs. Haemolysis will take place by altering the physical or chemical properties of any one of the three constituents which form the membrane: protein in imbibition, lecithin in imbibition, cholesterin.

Haemolysis can thus be produced by the following conditions:

(1) Adsorption of the lipoid mixture by substances which adsorb it more strongly than the protein network. Example: shaking with Kieselguhr.

(2) Altering the degree of imbibition of the protein network and the lipoid mixture by physical means. Example: freezing or heating.

(3) Altering the degree of imbibition by chemical means. Example: concentrated solutions of neutral salts.

(4) Altering the conditions under which cholesterin is dissolved in the lecithin solution ('demixing'). Example: water and hypotonic salt solution.

(5) Solution of the lipoids. Example: ether, alcohol, bile salts.

(6) Removal of one of the lipoids by combining with it or coagulating it. Examples: saponin, cobra venom, tetanolysin.

Conversely. the reason why a red blood corpuscle remains unaltered in physiological salt solution is not because there is an equal osmotic pressure inside and outside the cell, but because there is in that condition no alteration of the membrane. When water is added to a suspension of red blood corpuscles in salt solution, haemolysis results because there is first a weakening of the adsorbing power which attaches the lipoid mixture to the protein network, and this is followed by a 'demixing' of the lecithin-cholesterin solution.

Many of these conceptions are illustrated and supported by experiments: chiefly observations in dark ground illumination of haemolysis by different agencies. W. C.

**Hirsch, E. F. Changes in leucocytes and alkali reserve of blood in experimental infections.** *J. Infect. Dis.*, 1921, **28**, 275.

This paper deals with the question of the changes in the alkali reserve in the blood, in experimental infections in rabbits, with parallel observations on the variation in the number of leucocytes. The organisms employed were *B. coli*, *B. dysenteriae*, *B. typhosus*, *B. welchii*, *B. diphtheriae*, staphylococcus, pneumococcus, streptococcus and bacillus of Friedlander. Observations of the alkali reserve by van Slyke and Cullen's method, and of the leucocytes were taken at hourly intervals at first, when it was found that within a period of 2 to 4 hours there was a leucopenia and a diminution in the blood alkali reserve. Then follows a rise in the number of leucocytes and a return to normal of the alkali reserve. The minimal and maximal alkali reserve levels were reached after a corresponding leucopenia and leucocytosis. The author suggests that the diminution of the alkali reserve or the factors associated with this diminution may afford the chemical stimulus necessary for the subsequent leucocytosis. W. B.

**HEKTOEN, L.,** and **CORPER, H. J.** **The effect of mustard gas (Dichlorethylsulphid) on antibody formation.** *J. Infect. Dis.*, 1921, **28**, 279.

Many observations have been made on mustard gas since 1917, when it was used by the Germans at Ypres. The discovery by Krumbhaar and Krumbhaar that it exerts a direct toxic action on the marrow led the present authors to study its effect on antibody formation. Injected intravenously, in amounts varying from 0·005 to 0·0001 c.cm. a few days before or coincident with the intraperitoneal injection of sheep blood into rabbits, it had a restraining effect on the production of specific haemolysin and precipitin as compared to controls which received sheep corpuscles alone. Even when given several days after the antigen there was still an appreciable effect. Similar effects were observed in dogs subsequently injected with sheep blood or rat blood. A number of leucocyte counts in dogs poisoned with mustard gas are given. At first there is a decided leucocytosis, but this is followed by a great leucopenia. During the leucocytosis the Arneth classification method shows a moderate shift to the left followed by a shift to the right when leucopenia sets in and may reach almost a total absence of leucocytes 1 and 2 shortly before death. These results tend to place mustard gas among the leucotoxic agents like benzene, thorium X, and X-rays.
W. B.

**CORPER, H. J.,** and **RENSCH, O. B.** **The effect of mustard gas (Dichlorethylsulphid) on experimental tuberculosis.** *J. Infect. Dis.*, 1921, **28**, 286.

The effect of mustard gas in creating a disposition to pulmonary tubercle or in unmasking a lesion already latent has been widely accepted as a clinical belief. The present authors have made a study of the experimental side of the question. They found that mustard gas dissolved in 25 per cent. glycerol is bactericidal towards virulent human tubercle bacilli after an exposure *in vitro* of at least half an hour to 0·1 per cent. Mustard gas in 0·1 per cent. strength in 25 per cent. glycerol containing virulent T.B. and injected immediately subcutaneously into guinea-pigs entirely prevented the development of a progressive tuberculosis. In amounts which were non-lethal it had, however, no appreciable effect on the amount of tuberculosis in guinea-pigs already infected with T.B. W. B.

**JORES, L.** Experimentelle Untersuchungen über die Einwirkung mechanischen Druckes auf den Knochen. [**Experimental investigations on the influence of mechanical compression on bones.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **66**, 433.

Compression of bone tissue gives rise to a physiological stimulus which as long as it lasts hinders the growth of bone and causes its reabsorption as well as its substitution with connective tissue. As soon as the pressure is removed the same stimulus causes a proliferation of bone tissue to take place in that part of the bone which had been submitted to the compression. A disappearance of bone tissue in the case of pathological compression atrophy will therefore take place only when the pressure is permanent or when the periods of compression last longer than those through which pressure is removed. A proliferation of bone tissue will only take place in the opposite conditions, of periods of compression shorter than those free from pressure. C. d. F.

**Mattirolo, G.**, e **Bertolotti, M.** Sopra una malformazione rara dell'estremo cefalico della colonna vertebrale. [**On a rare malformation of the cephalic end of the vertebral column.**] *Gior. d. R. Accad. di med. di Torino,* 1920, **83**, 3.

In the case observed by the authors all cervical vertebrae were absent and their place taken by an almost amorphous bony mass measuring about 5 to 6 cm. in length. This mass was solidly fixed to the first two dorsal vertebrae, which also were fused together. The ribs, which were normally formed and of the usual number, reached the base of the cranium so that the subject had practically no neck. This total absence of the cervical spine appears to be an extremely rare malformation, of which a similar case was briefly described by R. O. Meisenbach (*Am. J. Orthop. Surg.* 1913, **10**, 647). But the only complete paper on the subject is that of Klippel and Feil (*Nouvelle Iconogr. de la Salpêtrière,* 1912, **25**, 223), where the literature and pathogenesis of the form are fully discussed.

C. d. F.

**Lewis, W. H.**, and **Webster, L. T.** **Giant cells in cultures from human lymph nodes.** *J. Exper. M.*, 1921, **33**, 349.

During an investigation on cultivation from normal and pathological human lymph glands in autogenous or heterogenous human plasma, the authors saw giant cells with a marked resemblance to those found in tuberculosis. They migrated out from grafts of normal and tuberculous glands from acute and chronic lymphadenitis, from Hodgkin's disease, and from a metastatic sarcoma. It was believed that the giant cells were similar in structure to the large wandering cells and probably derived from them, although in what manner was not clearly made out. The evidence was in favour of the view that they arise by amitosis of the nuclei without subdivision of the cytoplasm, which increases in bulk. They contained a large central area of more or less granular character and probably consisting of dead material, the waste products of metabolism and of digested foodstuffs. The central area was surrounded by a zone of fat globules in which the nuclei, 2 to 60 in number, were embedded. Mitochondria were numerous and usually in the form of wavy or curly threads. The whole giant cell was enveloped in a clear homogeneous ectoplasm. Four plates accompany the paper.

W. B.

**Musumeci, G.**, e **Di Macco, G.** La 'perspiratio insensibilis' attraverso le cicatrici cutanee e la cute di arti paretici. [**On insensible perspiration through cutaneous scars and the skin of paretic limbs.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 252.

The insensible perspiration through lupus scars is smaller than through the normal skin, and appears to take place by means of a simple process of diffusion of water through the layers of the newly formed connective tissue. On the skin of paretic limbs the insensible perspiration is greater than normally. The section of the sciatic nerve and its degeneration in consequence of a central lesion cause, in rabbits, the insensible perspiration to increase at the surface of the corresponding limbs. This insensible excretion of water through the skin of paretic or paralysed limbs also appears to occur through a simple process of diffusion and without any participation of the sweat glands.

C. d. F.

**Busacca, A.** Studi sulla curva di accrescimento della cellula gangliare dell'uomo. [**On the growth-curve of the human spinal ganglion-cell.**] *Gior. d. R. Accad. di med. di Torino*, 1920, **83**, 101.

Investigations were carried out on the fifth cervical ganglion of man from the eighty-seventh day of intra-uterine life to the eightieth year of age, and showed that the volume of ganglion cells continues to grow until about the thirtieth year of age, viz. until the body has generally reached its maximum weight. From that time onward the volume of ganglion cells diminishes. This is considered by the author as a phenomenon of senility and as a confirmation of the opinion of those who admit that senility is strictly connected with development and growth, and that the former begins as soon as the latter have reached their highest point. C. d. F.

**Gentili, A.** Sull' attività secretiva della preipofisi in gravidanza. [**On the secretory activity of the anterior lobe of the pituitary body during pregnancy.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 286.

Investigations were carried out by means of over 100 pituitary bodies collected from cows at different periods of pregnancy, as well as on many specimens from nulliparous animals. The results obtained are in great part a confirmation of well-known facts, and may be summarized as follows: The anterior lobe of the pituitary body increases progressively in size and weight from the beginning to the end of pregnancy. Whilst the average weight of the hypophysis of nulliparous cows is from 135–140 mgm., it already reaches 170 mgm. at the beginning of a first pregnancy, increasing up to 350 mgm. at the end of it. In cows of the same body-weight but multiparous, the weight of the pituitary body may increase from 310 up to 460 mgm. This means that in proportion to the body-weight that of the hypophysis grows from 1 : 100,000 in nulliparous cows to 1 : 50,000 at the end of the pregnancy in multiparous animals. Histologically the anterior lobe of the pituitary body of pregnant cows forms an excellent material for the study of the so-called gravidic cells, the chief function of which appears to be the secretion of a progressively increasing amount of lipoid substances, belonging, according to the author, to the phosphatides. Another feature of the anterior lobe of the pituitary body during pregnancy is the production of great quantities of colloid material, with the secretion of which the chromophobe cells appear to be chiefly concerned. C. d. F.

**Torraca, L.** Le alterazioni delle cellule nervose dei plessi parietali del tubo gastro-enterico come conseguenza di interventi chirurgici. [**Lesions of nerve-cells of parietal plexuses of gastro-enteric canal in consequence of surgical interventions.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 226.

The nerve-cells of the parietal plexuses of the stomach and intestine appear profoundly altered whenever their walls have undergone lesions of traumatic, inflammatory, or circulatory character. The alterations of nerve-cells generally consist of swelling or shrinking of their cytoplasm, formation of vacuoles, chromatorhexis, and more seldom chromatolysis. Nuclei appear sometimes swollen and less stainable, sometimes shrunk and pycnotic. In the case of wounds of the walls of the stomach or intestine, alteration of nerve-plexuses can be traced to a remarkable distance from the wound. In the case of adhesions of tracts of the intestine, or when this is surgically detached from the mesentery, altered nerve-cells are found only in the diseased or injured portions. An alteration of nerve-cells can be seen also in the wall of dilated intestinal loops above points of stenosis. Widespread and most severe alterations can be observed in cases of acute suppurative peritonitis. Particularly in the case of adhesions and peritonitis the lesions of Auerbach's plexus are more severe than those of Meissner's plexus. The results of the histopathological investigations are in agreement with the conclusions drawn from the functional examination of the intestine after various surgical interventions. C. d. F.

**Salvioli, G.** Contributo alle conoscenze istopatologiche nella lebbra. **[On the histopathology of lepra.]** *Sperimentale. Arch. di biol.*, 1920, **74**, 171.

Investigations were carried out on various organs, but particularly on the liver and spleen from two cases of **lepra tuberosa.** The following points are particularly emphasized by the author: Leprosy frequently gives origin to a form of cirrhosis of the liver and, to some extent, also of the spleen. The connective tissue proliferation and infiltration of such organs have often the features of the leprous granuloma, and are characterized by extensive degenerative phenomena chiefly consisting of accumulations of fatty and lipoid materials, which are mostly ingested by macrophages and other infiltration cells. Besides this fatty degeneration one can sometimes observe the presence of remarkable quantities of a granular, pigment-like material probably belonging to the group of melanins. This pigment is generally found in the foci of leprous infiltration either without or within the same scavenger cells containing fatty materials, and should be considered as 'the expression of a melanosis of toxic origin'. The degenerative phenomena observed in the liver may be considered, according to the author, as a lesion sufficiently characteristic to be used for the differential diagnosis between lepra and tuberculosis and, up to a point, between lepra and syphilis. The *B. leprae* stainable in internal organs, such as the liver and spleen, do not appear to be so acid-fast as those seen in the skin of the same subjects.
C. d. F.

**Schlagenhaufer, F.** Über Wirbelkörper-Schwund (Osteolysis). **[On the disappearance of vertebral bodies (osteolysis).]** *Beitr. z. path. Anat. u. z. allg. Path*, 1920, **66**, 483.

In a former communication (*Arb. a. d. Obersteiner'schen neurol. Inst. Wien*, 1907, **15**, 310) the author had described a case of compression myelitis due to the complete disappearance of the 9th dorsal vertebral body. The peculiarity of that case consisted in the absence of any apparent cause to which such a disappearance could have been attributed. It was consequently supposed to be a case of Kümmel's disease (traumatic spondylitis), the traumatic factor having, perhaps, been so slight as to have entirely escaped the attention and memory of the patient in whose clinical history no mention of the supposed trauma could be found. Since the publication of that first paper the careful post-mortem examination of the vertebral column in cases of gibbosity, with or without compression myelitis, has enabled the author to observe three other cases of this peculiar and rather inexplicable affection. These are now published by Schlagenhaufer, together with a summary of his earlier observation, and with a fifth case in many ways similar to the others.

The first four cases—three men aged 64, 55, and 54, and a woman aged 58—were all characterized by the isolated disappearance of the body of one vertebra. The affected vertebrae were—in one case the 9th dorsal, in two cases the 2nd lumbar, and in one the 7th dorsal, but in this last the affection had also spread to the body of the 8th dorsal. The supposition of a congenital malformation having had to be discarded for many clinical and anatomical reasons, the most thorough macroscopic and microscopic search was made for traces of well-known pathological processes such as tuberculosis, tumours, syphilis, spondylitis, osteomalacia, &c., but it was attended by negative results. The histological investigation of the small remains of the vanished vertebral bodies and of the bodies of the neighbouring vertebrae only led to the conclusion that a process of re-absorption of bone tissue had taken place, though not through the ordinary agency of the osteoclasts. In the microscopic preparation one could see either bone lamellae of normal aspect or fragments and clumps, the bony nature of which was revealed by the presence of a few bone-corpuscles. The affected areas looked like bone decalcified and more or less dissolved by some strong chemical agent. This suggested the idea that the origin of the process should be looked for in a sort of spontaneous decalcification of bone lamellae followed by their progressive re-absorption, ending ultimately in their complete disappearance. That this was probably the case was proved by the histological examination of the kidneys, in which unmistakable traces of an elimination of calcareous salts were found.

The fifth case was particularly interesting because of its acute course and extension of the affection to various bones. The patient, a woman aged 44, entered the Kaiserin Elisabeth Hospital on October 5, 1916, and there died, apparently of decubitus, on November 27 of the same year. She had never suffered from any important disease, but for about six months had complained of pains on both sides of the thorax. Latterly, the pains had become more acute and localized at about the level of the inferior dorsal and lumbar vertebrae. She could only find relief from her pains by lying in bed. A physical examination of the patient revealed only the presence of a gibbosity at the level of the 7th, 8th, and 9th dorsal vertebrae. This had been first observed by the patient about two months before her admission into the hospital. Here her condition became gradually worse in so far that she could not move from bed, and that any movement caused pain. At the post-mortem the same osteolytic process described above was observed, but, instead of being limited to the body of one vertebra, it affected, though in various degrees, the bodies of the dorsal vertebrae from the 6th to the 12th and of all the lumbar vertebrae; it had, moreover, spread to some of the vertebral processes, to the bones of the pelvis, to many ribs, and to the sternum. The result of the histological examination was the same as that of the former four cases, so that the author felt justified in considering it as a more severe and acute form of the same disease.

Of the intimate cause of this peculiar spontaneous dissolution and re-absorption of bone tissue the author can say nothing. He only points out that, as far as he knows, no similar cases have ever been described, and that in his opinion they should be considered as quite different from the forms of famine-osteomalacia (Schlesinger) and famine-osteopathy (Porges and Wagner) observed in Vienna in 1919. But he does not entirely exclude the supposition of cases of Kümmel's disease, particularly since Schlesinger has pointed out that there are cases which are not originally traumatic, but start as troubles of trophoneurotic nature leading in the end to a form of bone re-absorption and softness. C. d. F.

**Bolaffi, A.** Duplice reperto istopatologico dell' ittero castrense; rapporti tra ittero infettivo spirochetico de atrofia giallo-acuta del fegato. [**Dual histopathological character of spirochaetosis ictero-haemorrhagica; relation with acute yellow atrophy of liver.**] *Sperimentale. Arch. di biol.*, 1920, **74**, 182.

Important histopathological differences were noticed by the author between the forms of spirochaetosis ictero-haemorrhagica observed in the Allied and ex-enemy armies and those which occurred on the Italian front from 1915 to 1917. While the cases seen in Italy were, as a rule, mild, those studied in the other European armies generally followed a more severe course. Histopathologically the Italian forms were characterized by fatty degeneration and necrosis of hepatic cells, and fatty degeneration of the tubular epithelium of the kidney, whilst in the cases which ended fatally in other countries more important alterations were found, such as an exudative nephritis with variously localized haemorrhages, a severe degeneration of the tubular epithelium of the kidney and of the parenchyma of the liver, accompanied in this organ by a more or less extensive exudation of polymorphonuclear leucocytes and sometimes by proliferative processes. Moreover, almost all authors describe an intense erythro-phagocytic reaction on the part of the haematopoietic organs, of which there is no record in the Italian communications of 1915–17. However, a character common to both forms (the Italian and European) has been the occurrence of a large number of subserous haemorrhages in almost every case.

From foreign observations it would appear that the question is still in doubt as to whether spirochaetosis ictero-haemorrhagica may produce the alterations characteristic of acute yellow atrophy, but in Italy they appear to have been more fortunate, because Gozzi and Morandotti (*Giorn. med. mil.* 1917, **65**, 671) have found the spirochaete in the organs of two patients who showed the classical lesions of acute yellow atrophy, and Bolaffi now publishes five cases of epidemic jaundice collected in the period 1915–17, but characterized histopathologically by degenerative changes in every way similar to those of acute yellow atrophy.

Cases of spirochaetosis ictero-haemorrhagica clinically and anatomopathologically identical with those observed in foreign countries occurred also in Italy, but in 1918, viz. when the Italian epidemic of infectious jaundice was dying out. One of these cases was recently published by Racchiusa (*Riforma med.* 1920, **36**, 273), and four are now described by Bolaffi, who considers them as resulting from the arrival of the French and British reinforcements on the Italian front.

In spite of the histopathological differences and of the fact of not having been able to find the spirochaete either in the 1915–17 or in the 1918 cases, Bolaffi comes to the conclusion that the Italian form of epidemic jaundice was probably of spirochaetic origin like the foreign one, 'but it must have been a virus with different pathogenetic properties and a steatogenous power generally not possessed by the foreign spirochaete'. As to the *B. paratyphosus* found in some cases of Italian spirochaetosis, the author thinks that it was probably due to a concomitant infection. C. d. F.

**Foot, N. C. Studies on endothelial reactions. II. The endothelial cell in experimental tuberculosis. III. The endothelium in experimental pulmonary tuberculosis.** *J. Exper. M.*, 1920, **32**, 513, 533.

The author claims that in his previous work in this series he showed that endothelial cells of capillary blood-vessels ingest nearly all the carbon of an intravenous injection of a lamp-black gelatin colloidal suspension. These endothelial cells thus labelled by contained carbon were identified as giving rise to the large mononuclear phagocytes of an inflammatory reaction in connective tissue induced by subcutaneous injection of agar. The present paper relates experiments on similar lines by which the author claims to show that the epithelioid cells of tuberculosis are derived from the endothelial cells of local small blood-vessels and not from fibroblasts or lymphocytes. A mixture of Higgins's ink and tubercle bacilli was injected subcutaneously into three rabbits at hourly intervals up to 30 hours. There seems to have been nothing histologically characteristic of tuberculosis in the resulting reaction so early as this. Great proliferation of wandering endothelial cells from the smallest vessels was noted. The endothelium of vessels with muscular walls seem to take little part in the process. Large carbon-containing cells like fibroblasts that were seen are said to be endothelial in origin because all the connective tissue cells of the part appeared to have been destroyed by the injections and so could not react.

In another experiment eight rabbits received Higgins's ink intravenously every third or fourth day and subcutaneous tubercle bacilli at varying periods up to 49 days. The large mononuclear cells and giant cells that composed the resulting tubercles and the endothelial cells of neighbouring vessels were full of carbon granules, lymphocytes in the tubercles being free from pigment. Though they are not the parents of the epithelioid cells, fibroblasts may be the parents of the cells which tend to wall off the lesions. There is a discussion of the literature on the subject of tubercle formation.

In the third paper (p. 533) the author discusses previous work on this subject, and holds that if Sewell had used a colloidal suspension of carbon (such as Higgins's ink or McJunkin's preparation) instead of a mechanical suspension of Indian ink, his conclusion that the epithelioid cells of pulmonary tuberculosis are alveolar epithelial cells would have been different. Dr. Foot points out that the epithelium of the alveoli and infundibula of the lung is composed of three types of cell. One type closely resembles the vascular endothelium. He claims that these originate in the endothelium of alveolar capillaries because they take up carbon, and that they are clumped in the normal lung on the surface and in the cavity of the alveoli as potential phagocytes. The main conclusion of his work is that these cells (which he has classified as one type of alveolar epithelial cell), together with continuously migrating capillary endothelial cells, are the cells which proliferate to form the epithelioid cells and giant cells of the lesions of experimental pulmonary tuberculosis. His next conclusion states that the alveolar epithelium takes no active part in the process.

Description is given of findings in the lungs of three rabbits injected with pigments only. The carbon was always introduced intravenously. Carbon was found in mononuclear cells of endothelial type and a little in occasional polymorphonuclear leucocytes, never in true alveolar epithelium. Intratracheal carmine was found also in the mononuclears and but little in the epithelium. Tissue reaction to pigments alone was slight and transitory.

Series of rabbits received intravenously Higgins's ink and were killed at nine periods of time, varying from 1 hour to 7 days, after intratracheal injection of tubercle bacilli and lithium carmine. Findings up to the fourth day included swelling and mitosis in capillary endothelium and a few bacilli in desquamated epithelium. After this, small intrapulmonary lymph nodes are found to contain tubercles composed of mononuclear cells, some containing carbon. Later, similar tubercles form in the alveoli, their syncytia and mononuclear cells containing carbon, carmine, and tubercle bacilli.

By the fifth day conglomerate areas are formed. The fibroblasts begin to form bands of connective tissue between the masses of endothelial cells. There is also gelatinous exudate and fibrin. Lymphocytes appear in the lesions about the sixth day.

Wandering cells containing carbon, tubercle bacilli, and carmine were found in the lymphatics. Dr. Foot reiterates that the presence of carbon in considerable amount in a cell is proof of the cell's origin from capillary endothelium. To get bacilli and carmine the cell must have been into the alveolar cavity. Therefore these cells must migrate into the alveoli from the vessels; they then carry bacilli along the alveolar passages and along the lymphatics, thus spreading the infection. This behaviour, so unlike that of epithelium, is further proof of the endothelial origin of these cells.

W. W. W.

## BIOCHEMISTRY

**Hári, P.** Über die Lichtabsorption des reduzierten Haemoglobins. [**The light absorption of reduced haemoglobin.**] *Biochem. Ztschr.*, 1921, **115**, 52.

Hufner's experiments upon the light absorption of reduced haemoglobin have been repeated with improved technique. The maximum absorption is found to be at 553·3.

R. A. P.

**Feigl, J.** Über das Vorkommen und die Verteilung von Fetten und Lipoiden im Blute nach Blutentziehung. Chemische Beiträge zur Kenntnis des Lipämiegebietes, VII. [**On the appearance and the distribution of fats and lipoids in the blood after bleeding. Chemical contribution to the knowledge of lipaemia.**] *Biochem. Ztschr.*, 1921, **115**, 63.

Using Bloor's method the author has confirmed the results obtained by Horiuchi upon the changes of fatty bodies occurring in the blood after bleeding. He has also extended these to a number of clinical cases in which blood has been lost during operation. In the main the results agree with the animal experiments. A lipaemia is brought on lasting a matter of three days. The greatest change occurs in the neutral fats and represents a mobilization of fat. Lesser changes in the lecithin and cholesterin bodies also occur. The shedding of as little as 200 c.c. of blood may initiate a lipaemic complex, according to the author.

R. A. P.

**Macleod, J. J. R.** **The concentration of lactic acid in the blood in anoxaemia and in shock.** *Am. J. Physiol.*, 1921, **55**, 184.

The percentage of lactic acid in the blood was determined in conditions of anoxaemia. The acid increases in the blood after a considerable interval of time (10–20 minutes) after the onset of anoxaemia. This shows that the appearance of an excess of lactic acid has no relationship to the symptoms of anoxaemia (stimulation of the respiratory centre), as was formerly believed but as is now no longer maintained. It is suggested that the excess of lactic acid in anoxaemia may perform the function of assisting in the neutralization of the relatively increased base which results from the blowing off of $CO_2$ from the blood, this being dependent upon stimulations of the respiratory centre by the oxygen deficiency.

Observations were also made on the increase of lactic acid in the blood in various stages of experimental shock. The acid appears in excess in shock only after the respiratory and circulatory functions have become so greatly depressed that a condition of anoxaemia exists long after the condition of shock has become definitely established. The appearance of the acid has therefore no causal relationship to the establishment of the condition. W. C.

**Ege, R.** Die Verteilung der Glucose zwischen Plasma und roten Blutkörperchen. Zur Physiologie des Blutzuckers, IV. [**The distribution of glucose between plasma and red blood corpuscles. On the physiology of the blood sugar.**] *Biochem. Ztschr.*, 1921, **111**, 189.

A modification of Bang's micro-method has been used for analysis. The blood-corpuscles of the goat, ox, and rabbit contain no glucose. Those of the dog contain one-third of the concentration in the plasma, and those of man about three-quarters of the amount in the plasma. Glucose added to the blood of the goat, ox, rabbit, and dog remains in the plasma. The impermeability to glucose is destroyed by treatment with formalin, though after this treatment the partition of glucose between corpuscles and plasma is not identical. Glucose added to human blood is distributed variably between plasma and corpuscles. The author states that he has found that human blood corpuscles from hirudinized blood are also permeable to glucose, which is the opposite result to that found recently by Falta and Richter-Quittner. He discusses at some length the conditions under which glucose exists in the corpuscles. R. A. P.

**György, P.** Notiz zur Kenntnis der Senkungsgeschwindigkeit von roten Blutkörperchen. [**The sedimentation of blood corpuscles.**] *Biochem. Ztschr.*, 1921, **115**, 71.

Fåhraeus has shown that under normal circumstances the rate at which corpuscles sink is constant for men. The corpuscles of women sink quicker and there is a comparatively large change in pregnancy. Plaut has found similar increased rates of sedimentation in certain diseases, such as paralysis and arteriosclerosis. The increased rates of sinking can only be observed in the plasma and are not found in the serum. The author has found that the sinking velocity of the washed corpuscles of the ox is lowered by the addition of a lipoid soluble substance such as lecithin, ethyl, and propyl alcohol. Most other substances, both electrolytes and non-electrolytes such as quinine have no effect upon the rate of sinking. R. A. P.

**Coulter, C. B. The equilibrium between haemolytic sensitizer and red blood cells in relation to the hydrogen-ion concentration.** *J. Gen. Physiol.*, 1921, **3**, 513.

In a salt-free medium, the proportion of sensitizer combined with cells reaches a maximum of nearly 100 per cent. at $P_H = 5{\cdot}3$, and a minimum of about 5 per cent. at $P_H = 10$. Sodium chloride increases the proportion combined except in the neighbourhood of $P_H = 5{\cdot}3$, where its effect is absent. There is a reversible equilibrium between that free and combined. The combination is related to the iso-electric point of the sensitizer, and undissociated molecules only of sensitizer combine with the cells. W. M. B.

**Erlanger, J. Studies in blood-pressure estimation by indirect methods. III. The movements in the artery under compression during blood-pressure determinations.** *Am. J. Physiol.*, 1921, **55**, 84.

A detailed experimental investigation of the mechanics underlying the clinical methods of blood-pressure determination by the compression of arteries. W. C.

**Aszódi, Z.** Beitrag zur Kenntnis der chemischen Wärmeregulation des Säugetiers. II. Über künstlich erzeugte winterschlafähnliche Zustände an Mäusen. [**Contribution to our knowledge of the chemical heat regulation of mammals. II. On the artificial hibernating state in mice.**] *Biochem. Ztschr.*, 1921, **113**, 70.

It seems from this paper that the difference between the warm-blooded and cold-blooded animal is not quite so wide as has hitherto appeared to be the case. Warm-blooded animals in general show a rise in metabolism as the outside temperature sinks—the chemical heat regulation. The author here shows that when the outside temperature falls below 19° C. for a starving white mouse, and below 13° C. for a well-fed one, the chemical regulation fails. The body temperature sinks considerably and the animal becomes to all intents and purposes cold blooded. This state is ushered in by a torpid condition of the animal. The torpid state soon gives way, as the temperature is lowered, to a state of hibernation; in which the metabolism is lowered to one-seventh of the normal value. The respiratory quotient sinks below 0·7. If this state is not maintained for more than 24 hours, the animal may be able to recover completely. The auther regards this artificial hibernation and the true hibernation as differing from one another only quantitatively. R. A. P.

**Rothlin, E.** I. Experimentelle Studien über die Eigenschaften überlebender Gefässe unter Anwendung der chemischen Reizmethode. [**Experimental studies of the properties of surviving vessels under treatment with chemical stimuli.**] II and III. Experimentelle Untersuchungen über die Wirkungsweise einiger chemischer, vasotonisierender Substanzen organischer Natur auf überlebende Gefässe. [**Experiments on the effect of some chemical, vasotonic substances of organic nature upon surviving blood-vessels.**] *Biochem. Ztschr.*, 1920, **111**, 219, 257, 299.

These three papers are concerned with the problem of vasoconstriction and vasodilatation. The author has developed the method of studying isolated blood-vessels such as mesenteric, limb and renal arteries of the horse, cow, and sheep. He has also used a method of perfusion in the case of the pithed frog for the lungs, splanchnic region, and hinder extremities.

Isolated arterial strips kept in Ringer's solution saturated with oxygen undergo three phases of change. First, the vessel dilates, reaching its maximum state of distension slowly towards the end. It then contracts to a second stage of mean tone, which may last many hours, to be followed by a more severe state of contraction, which is the final phase. Experiments were made upon vessels in a state of 'mean tone'. For the maintenance of this state, the optimum temperature is body temperature. It is highly dependent also upon oxygen pressure. Increase of oxygen causes increased tone, diminution the reverse; the effect is independent of the control of the central and autonomic nervous systems. In such isolated strips rhythmic changes of tone are often observed though the rhythm shows great variation in the form, frequency, and amplitude of contraction. Oxygen again is an important factor in both the starting and maintenance of rhythm, though rhythm can be sometimes started by vasoconstrictor substances. Vasodilator substances never start rhythmic activity and inhibit any that may be present. Though the rhythm in isolated strips is undoubtedly a physiological property of the vessels, it cannot be said to fulfil the function of a 'peripheral heart'.

The author finds that there is present a vasoconstrictor substance in serum (in confirmation of other work), and in defibrinated blood, but not in oxalated blood. The substance appears as the result of coagulation. It is not adrenalin. It is heat stable, dialysable and soluble in alcohol, and apparently present in the circulating blood. Adrenalin generally shows a contractile effect upon isolated vessels, though there are exceptions. Renal vessels, for instance, are constricted by strong doses, but dilated by weak ones. There are also anomalies in the case of heart-vessels. In the case of the lung, isolated horse and ox arteries only show contraction, and that a weak one, upon treatment with adrenalin. Perfusion of the lung of the pithed frog, however, shows dilatation for weak doses and contraction for strong ones. According to the author the discrepancy is to a certain extent attributable to the fact that isolated preparations of necessity must be only from the larger lung vessels.

Histamin pituitary extract, and lienin (the active principle of the spleen) generally give contraction in the isolated blood-vessel preparations. Exceptions are to be found in the case of the lung and splanchnic vessels of the frog. In these cases the double result of a dilatation for weak doses, followed by contraction for stronger, tends to appear in the perfused organs of pithed frogs. The author discusses at some length the general views of vasodilator nerves, and Elliott's views of the essential similarity of effect between adrenalin and the sympathetic system. In connexion with this it is interesting that certain isolated vessels (notably renal) can respond to adrenalin both by vasodilatation and vasoconstriction under slightly different strengths of dose. R. A. P.

**van Slyke, D. D. The carbon dioxide carriers of the blood.** *Physiological Reviews*, 1921, **1**, 141.

This article appears in a new quarterly journal published by the American Physiological Society, of which a complete prospectus for the year has already been issued. The main purpose is to keep workers in touch with contemporary research. It will endeavour to give summaries of recent advances in knowledge in physiology, embracing biochemistry, biophysics, experimental pharmacology, and experimental pathology. The programme for the year is a very varied one and embraces such subjects as undernutrition; contributions of war surgery to the physiology of the central nervous system, gastric secretion in health and disease, anaphylaxis, &c. The reviews ought to be of service, not only to the laboratory worker, but to the clinician who desires to know the most recent physiological views regarding the phenomena of pathological conditions.

The present review deals with the question of the transport of $CO_2$ in the blood, and the means by which this is brought about without appreciable changes in the reaction of the blood. The author discusses at some length the mathematical basis of physico-chemical equilibrium in the blood. For practical purposes, we can limit ourselves to two forms of $CO_2$, one as $H_2CO_3$ and the other as $HBCO_3$ (where $B =$ a monovalent base such as Na or K). The balance between $H_2CO_3$ and $BHCO_3$, the ratio $\frac{H_2CO_3}{BHCO_3}$, is a measure of the hydrogen-ion concentration of the blood. The addition of $CO_2$, or the removal of $CO_2$, in quantity from such a system as the above (if no other substances were present) would result in changes of blood-reaction quite incompatible with life. These changes are prevented by the presence in the blood of buffer substances. The important buffers in the blood are the bicarbonates, the phosphates, and the alkali salts of the proteins. The alkali salts, constituting the buffers of the blood, act as 'reservoirs of alkali', giving up alkali to neutralize the carbonic acid or other acid that may enter the blood. L. J. Henderson has calculated mathematically the relations which may be expected to hold under these conditions from a consideration of the laws of mass action, and has shown that the actual efficiency of the carbonates and phosphates as buffers is nearly maximal at the blood-reaction, though there is a slight increase in efficiency as the reaction becomes slightly more acid than the blood. Interestingly enough, it has been recently shown by Campbell and Poulton that the dissociation constant of the oxyhaemoglobin is at its greatest buffering efficiency at the reaction of the blood, another interesting example of the biological adaptation of oxyhaemoglobin.

van Slyke then defines 'a carbon dioxide carrier of the blood in the physiological sense as a constituent of the blood which increases the amount of $CO_2$ that may be taken up by arterial blood with a change in reaction equal only to the difference between arterial and venous blood'. He gives an illustration in detail as to how a buffer salt is able to do this. The important experiments of Joffe and Poulton show that under the influence of changes in reaction the richly buffered cells are able to transfer their buffer effect to the poorly buffered plasma, so that the latter, when in contact with the cells, becomes as efficient a $CO_2$ carrier as the former. The cell buffers themselves are chiefly haemoglobin and phosphate, of which neither diffuse out into the plasma. The mechanism by which the change is effected is a diffusion of Cl, and to a lesser extent $SO_4$, into the corpuscles, with increasing pressure of $CO_2$. At the same time there is a change in the acidity of haemoglobin. Oxyhaemoglobin is a stronger acid than reduced haemoglobin. van Slyke regards oxyhaemoglobin as the chief carrier of $CO_2$ in this sense, as it is also of oxygen in the blood. Of the alkali furnished to neutralize $CO_2$ entering the venous blood, he calculates that 80–95 per cent. comes from the haemoglobin. The greater part of this would be set free when the relatively strong acid oxyhaemoglobin is changed to the weaker haemoglobin. The cells themselves are permeable to HCl and $H_2CO_3$, and it is by the mediation of these that the reserves of buffer alkali in the cells can be used to maintain constancy of reaction of the blood, although the buffers themselves do not actually leave the cells.

The above is a necessarily short abstract of a most excellent review, which should be read by all those interested in the subject.

R. A. P.

**Peters, J. P., Barr, D. P., and Rule, F. D. The carbon dioxide absorption curve and carbon dioxide tension: I. Of the blood of normal resting individuals. II. Of the blood in cardiac dyspnoea. (Peters, J. P., and Barr, D. P.); III. Of the blood in severe anaemia. (Barr, D. P., and Peters, J. P.)** *J. Biol. Chem.*, 1921, **45**, 537.

The titles of these three interesting papers indicate their general purport. The authors have made an extensive study of the blood of normal and certain pathological individuals from the special point of view of the respiratory function of the blood. For this purpose they have made estimations of $CO_2$ content and oxygen capacity of arterial and venous blood and followed this with determinations of the $CO_2$ absorption curve of the blood in question. Measurements of the alveolar $CO_2$ by the method of Haldane and Priestley were also made. For the normal persons studied, in agreement with previous observers, they have found the limits of $CO_2$ capacity of normal blood, when compared at 40 mm. tension and 37·5° C., to be 43–56 vols per cent. The curves of individuals differ both in height and shape, but they remain very constant for the same individual, confirming the conclusion of Christiansen, Douglas, and Haldane. If the hydrogen-ion concentration of the blood is calculated by application of the formula $H_2CO_3/NaHCO_3$, the surprising result is reached that the normal hydrogen-ion concentration of the blood may vary for different individuals by as much as 0·2 $P_H$. Further, the alveolar $CO_2$ tension may be 10 or 11 mm. lower than the $CO_2$ tension of arterial blood, indicating that the alveolar $CO_2$ tension does not necessarily give the arterial $CO_2$ tension, as has been previously supposed.

A study of 7 cases with cardiac decompensation and dyspnoea gave interesting results. In 3 of them low $CO_2$ absorption curves were found, two of which returned to a normal level as compensation was re-established. These cases had cyanosis with little dyspnoea. The reduction indicated by the low absorption curves was not apparent in the plasma. Thus the plasma method of determining the alkali reserve cannot be applied in cases where there is an accumulation of $CO_2$ in the venous blood. Whole blood must be used in such cases, though by a previous treatment with alveolar $CO_2$ the difficulty can be to a certain extent removed. There was a notable difference between the arterial and alveolar $CO_2$ tension, viz. 13–19 mm. in these cases. They think cardiac dyspnoea is produced owing to the fact that a larger ventilation is needed to effect a normal $CO_2$ elimination. This result is mainly due to an impairment of the pulmonary mechanism for the exchange of gasses between the blood and the outside air, leading to the necessity of a greater difference in $CO_2$ pressure between the blood in the lungs and the alveolar air. Diminution in the circulation rate may also be a factor. Some cases show a real reduction of available alkali. $CO_2$ absorption curves of blood from six patients with severe anaemia showed a flatter curve than normal, approximately more to the plasma curve. This was not completely explained by the change in haemoglobin content of the blood. The conclusion to be drawn from this is that changes in $CO_2$ tension produce little changes in $CO_2$ content in severe anaemias, though large changes in hydrogen-ion concentration. R. A. P.

**Peters, J. P., jun., and Barr, D. P. Studies of the respiratory mechanism in cardiac dyspnoea. I. The low alveolar carbon dioxide of cardiac dyspnoea. II. A note on the effective lung volume in cardiac dyspnoea. III. The effective ventilation in cardiac dyspnoea.** *Am. J. Physiol.*, 1920, **54**, 307, 335, 345.

During the dyspnoea of cardiac decompensation the effective volume of the lungs is diminished. The alveolar air obtained from such patients by Haldane's method is functionally true alveolar air or exchange air—that is to say, it is the only air which can be functionally effective in the elimination of $CO_2$ from the body. But it is doubtful whether the normal relation between the $CO_2$ tension of alveolar air and that of arterial blood holds good in cardiac decompensation.

In dyspnoeic cardiac subjects the percentage of $CO_2$ in the alveolar air is low. This necessitates a larger effective ventilation to accomplish $CO_2$ elimination, so that the cardiac patient exhibits hyperpnoea even when the metabolism is normal. As long as he lies quietly in bed, this involves an increase in the rate of respiration without very great changes in the volume of each respiration. Under these circumstances the low effective lung volume which accompanies decompensation is therefore not an important factor in the causation of dyspnoea. It probably comes into play when the $CO_2$ production is increased. Under the stimulus of $CO_2$ the volume of the tidal air increases in cardiacs and in normal individuals. This increase is, however, in proportion to the vital capacity. And since in decompensated cardiacs the vital capacity is greatly diminished, the maximum volume of respiration is greatly limited and the cardiac patient cannot respond as efficiently to the stimulus of $CO_2$ by increasing his ventilation, so that marked subjective dyspnoea results.

This dyspnoea explains itself, therefore, as the result of two factors: the low $CO_2$ percentage in the 'effective' or 'alveolar' air makes an increase in ventilation essential. This factor is active under all conditions while the patient is decompensated. The diminished effective lung volume makes any large increase difficult or impossible. This second factor exerts its chief influence when the $CO_2$ production in the body is increased.

W. C.

**Schneider, E. C., and Truesdell, D. A study of low oxygen effects during re-breathing.** *Am. J. Physiol.*, 1921, **55**, 223.

The Official Altitude Classification Examination of the Air Service, U.S. Army, is a low oxygen test in which the candidate is required to re-breathe 52 litres of $CO_2$ free air. Pulse-rate, blood-pressure, and respiration were determined. The test was terminated when the subject had reached the point of complete mental inefficiency, as tested by a psychologist, or when the circulation indicated oncoming syncope.

The authors have studied 1,050 out of 7,000 records and analysed them. The normal and abnormal responses in respiration, pulse-rate, and the systolic, diastolic, and pulse-pressures are presented by curves.

W. C.

**Brooks, M. M. Comparative studies on respiration. XV. The effect of bile salts and of saponin on respiration.** *J. Gen. Physiol.*, 1921, **3**, 527.

The rate of respiration of *Bacillus subtilis* is increased by sodium taurocholate in concentrations of 0·0000125 m. and decreased at and above 0·001 m. NaCl is antagonized by taurocholate in molecular proportions (1 part of the latter to 14,375 of the former). Saponin in 0·00005 m. to 0·001 m. decreases rate of respiration; and has no effect in lower concentrations.

W. M. B.

**Fries, J. A. The respiratory quotient and its uncertainty.** *Am. J. Physiol.*, 1921, **55**, 53.

It is pointed out that fermentative processes in the stomach introduce considerable errors in the estimation of the respiratory quotient, especially when the determinations are made over short periods.

W. C.

**Macleod, J. J. R. Periodic breathing and the effects of oxygen administration in decerebrate cats.** *Am. J. Physiol.*, 1921, **55**, 175.

In the course of observations on the breathing of decerebrate cats it was found that periodic breathing can be induced by a variety of ways, in all of which a deficiency of oxygen can be shown to be the ultimate cause of the condition. The arterial blood-pressure exhibits waves synchronous with those of the respirations, and occasionally there is vagus slowing during the rise of the curve.

Decerebration is not always followed by the same effects on respiration, the differences being dependent partly on the age of the animal and partly on the exact position at which the mesencephalon is cut. In some animals the breathing is irregular and spasmodic from the start, and the animals soon develop the symptoms of asphyxia with convulsive movements which terminate in death. Several, though not all, of these animals react in a remarkable way towards the administration of oxygen through a catheter in the trachea. The breathing, which previous to the administration of oxygen was inadequate to maintain life, became regular and the preparation was maintained for hours in normal condition.

These observations have an important bearing on oxygen therapy in man. They indicate that under certain conditions of breathing at atmospheric pressure, one of which is low blood-pressure, a sufficient supply of oxygen may not be carried to the respiratory centre to maintain its excitability.

W. C.

**Laqueur, E.**, and **Magnus, R.** (1). Über Kampfgasvergiftungen. III. Experimentelle Pathologie der Phosgenvergiftung. [**Poison gases. III. The experimental pathology of phosgene poisoning.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **13**, 31.

**Laqueur, E.**, and **Magnus, R.** (2). Über Kampfgasvergiftungen. V. Experimentelle und theoretische Grundlagen der Phosgenerkrankung. [**Poison gases. V. The therapy of phosgene poisoning.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **13**, 201.

These two papers form a very extensive contribution to the literature of poison gases. The experimental work was done under war conditions in Berlin, and the authors were assisted by a number of well-known clinicians, pathologists, and physiologists.

The first paper takes up the methods of investigation. All types of animals were used, and it appears from the results that man takes an average place in sensitiveness to phosgene gas. About 0·25 mgm. of the gas is sufficient to kill a cat. Of this amount only a small part is the active agent. The amount of the gas which is subjectively insupportable is 5–10 mgm. per cubic metre. After describing the well-known clinical phenomena connected with phosgene the authors have made a detailed investigation of the more intimate pathological conditions. There is an increase in weight and size of the lungs and pulmonary oedema. The cut surface of the lung is darker, and microscopically the alveolar epithelium is seen to be shed. Following this are toxic pneumonia foci with a broncho-pneumonia. In six days resorption is complete if recovery takes place; this of course only takes place when the gas concentration is small. The pulmonary exudate has approximately the same composition as blood plasma.

Section of the vagi does not influence the characteristic changes in the lungs, but there is much less formation of oedema and little change in the lungs if the section has been performed prior to exposure to the gas. This is due to putting out of commission the sensory branches of the vagus in the lungs.

An analysis of the respiration shows that phosgene influences breathing unfavourably by interference with the sensory nerves. The breathing becomes shallower.

Part of the danger of increased muscular effort after phosgene poisoning is due to the fluids in the lungs becoming frothy and so stopping the larger air-channels. The principal factor is the attempt to effect the greatly increased respiratory exchange due to muscular effort with a damaged lung. The respiratory products cannot be eliminated and the individual dies of asphyxia.

The toxic action of the gas cannot be attributed to general acid poisoning but is to be put down to the local action on the pulmonary epithelial wall. This action is probably due to phosgene *per se* and not to its decomposition products. The blood becomes more concentrated and viscous, adding in this way a difficulty to circulation; the oxygen of the blood sinks below normal value, especially in severe cases of poisoning; the carbon dioxide is kept nearly at a normal level, except in the very pronounced cases of poisoning where carbonic acid is retained. Death takes place by asphyxia with secondary failure of circulation. As in infectious pneumonia there is a retention of chlorides in the body.

Experiments with the isolated and perfused lung preparation showed that the principal primary effect of the gas was on the lung itself.

Fall of blood-pressure takes place, and an analysis of the factors involved leads the authors to conclude that it is due to circulatory hindrance in the lung itself. From the metabolic side an increase in total nitrogen and creatinin were noted. There is a (toxic ?) destruction of protein. (These experiments were done with 'Perstoff', perchlorformic methyl ester.)

The authors point out the opportunity which a study of phosgene poisoning offers of investigating many of the problems of pulmonary pathology.

The second paper is concerned with the therapeutics of phosgene poisoning and it is interesting to note that from the German side practically no therapeutic measures were suggested which were not tried very early in England. The paper is divided into sections dealing with general and specialized therapeutics intended to combat oedema, disturbances of respiration, blood concentration, circulatory failure, and after-effects.

It would appear that the use of calcium salts given subcutaneously (800 c.c. of a 1·0 per cent. solution) in man had some effect on oedema. In animals it was distinctly useful, reducing the mortality from 88·0 per cent. to 55·0 per cent. In these cases it was used early after poisoning. The results of using hypertonic sugar solution were not concordant in rabbits and cats, but are suggestive.

The principal agents in the early stages are complete muscular rest and fresh air. Oxygen is useful provided the concentration be not too high and administration not too prolonged. Morphine is distinctly contra-indicated. Codeine may be used.

In combating the increased concentration of the blood following oedema of the lungs venesection is the best means. The injection of isotonic salt solution is useful but the effect is fleeting. Venesection should not be followed by the injection of salt. In the treatment of cardiac conditions camphor and caffeine are the two best agents. Digitalis and strophanthine, if given should be administered intravenously and intra-muscularly, owing to the delay in absorption.

Apart from their interest in the pathology and therapeutics of phosgene poisoning, these two papers are highly instructive as a contribution to our knowledge of inflammation of the lungs. C. G. L. W.

**Holló, J.** Untersuchungen über Ursachen von Variationen in der Reaktion des normalen menschlichen Urins. [**Experiments on the source of variations in the reaction of normal human urine.**] *Biochem. Ztschr.*, 1921, **113**, 246.

This is a contribution to the power possessed by the kidneys of separating an acid urine from an alkaline plasma. In the case of individuals with normal kidneys, the intravenous injection of phosphate either as the acid or as the alkaline salt led to an increase of the acid phosphate in the urine. Dilution of the urine, on the other hand, produced by drinking water, led to the separation of more alkaline salt. R. A. P.

**Hedin, S. G.** Über proteolytische Enzyme im normalen und pathologischen Harne. [**On proteoclastic enzymes in normal and pathological urines.**] *Ztschr. f. physiol. Chem.*, 1921, **112**, 252.

The proteoclastic enzymes of urine have been investigated with respect to their action on (1) casein in alkaline solution; (2) Witte peptone in alkaline solution; (3) casein in acid (HCl) medium.

(1) Normal urine has either no action, or, at most, only the very slightest on casein in alkaline solution. In pathological conditions, for instance, during the fever of pneumonia, this action is very definitely greater, and is still more marked in cases of albuminuria.

(2) The hydrolysis of Witte peptone in alkaline solution is always effected by normal urine. During the stage of fever in pneumonia this action is increased, as is the case also in leucaemia, although here the action on alkaline solutions of casein is not correspondingly greater. In albuminuria the increase of action on peptone is strongly marked.

(3) Normal urine has a definite action on casein in acid medium but no regular increase in activity has been noted in pathological conditions.

H. W. D.

**Hume, E. M. Comparison of the growth-promoting properties for guinea-pigs of certain diets consisting of natural foodstuffs.** *Biochem. J.*, 1921, **15**, 30.

In continuance of experiments on guinea-pig scurvy various vegetables, milks, germinated seeds, and fruit juices were tried, both raw and cooked, to ascertain the amount necessary to prevent scurvy, and to ascertain the effect of cooking on fat-soluble A.

Those substances which promote growth are green cabbage, hay, and milk; no growth takes place with white cabbage, swedes, orange juice, or germinated peas. Cooking has little effect on the potency of the vitamine. A definite amount of the substances must be given to ensure normal growth.

C. G. L. W.

**Mackay, H. M. M. The effect on kittens of a diet deficient in animal fat.** *Biochem. J.*, 1921, **15**, 19.

Six weeks' old kittens, when fed on a diet which was adequate, but which was deficient in fat-soluble A, became emaciated and finally ceased growing. With younger kittens the results were more striking and gave an appearance like that seen in children suffering from coeliac disease. There was no evidence at rickets *post mortem.* C. G. L. W.

**Davey, A. J. Determination of the minimum doses of some fresh citrus fruit juices which will protect a guinea-pig from scurvy, together with some observations on the preservation of such juices.** *Biochem. J.*, 1921, **15**, 83.

During the war it was found that lime juice did not bear out its reputation for protecting troops from scurvy, while the fresh juices of oranges and lemons were highly efficient. It was also important to know whether the methods of preparation were responsible for the loss of anti-scorbutic powers. The authoress has made a careful examination of the antiscorbutic properties of many varieties of the fruits of the citrus family. Lemon and orange juice are four times as potent as fresh lime juice. Preservation with sulphides is only satisfactory when the juice can be kept at 0° C. The introduction of the oil of the rind gives more satisfactory results at 100 c.c. temperature. When the juices are exposed to higher temperatures, as they are in the tropics, no method has so far been successful. Cold storage of the fruit itself does not appreciably diminish its protective qualities against scurvy. C. G. L. W.

**Hume, E. M. Investigation of the antiscorbutic value of full cream sweetened condensed milk by experiments on monkeys.** *Biochem. J.*, 1921, **15**, 163.

Condensed milk diluted 1–4 is the equal of a similar volume of raw milk in antiscorbutic properties. The possible danger in its use for infant feeding is due to the fact that it is diluted to at least 1–8. C. G. L. W.

**Jephcott, H.**, and **Bacharach, A. L. The antiscorbutic value of dried milk.** *Biochem. J.*, 1921, **15**, 129.

Summer and winter milks were dried by the roller process and by the spray process. The preparations made by the roller process had antiscorbutic values about equal to the original raw milk. Neutralized milk was slightly lower in potency. The milk dried by the spray process was markedly deficient in the antiscorbutic factor. C. G. L. W.

**Hartwell, G. A. The effect of diet on mammary secretion.** *Biochem. J.*, 1921, **15**, 140.

The animals used for this study were rats. A definite litter of six was always employed, the mother fed on various diets and the effect on the litter observed. Weights of mothers and litters were recorded.

A difference of 100 per cent. may be observed in the weights of litters at the end of lactation, depending on feeding the mother on inadequate diet (bread) and an adequate one (bread and whole milk). Both extractives and protein tend to keep up the weight of the mother.

The mother can supply fat, fat-soluble A, water-soluble B, and the antiscorbutic factor.

The experiments emphasize the importance of the maternal diet in promoting the satisfactory growth of the breast-fed young. C. G. L. W.

**Schmiesing, T.** Die Verdauung von Säuglingsnahrung. [**The digestion of infants' foods.**] *Ztschr. f. physiol. Chem.*, 1921, **112**, 295.

Various milk mixtures were fed to a dog with a duodenal fistula whose cannula was situated directly opposite the opening of the lower pancreatic duct. They displayed no effect of any significance on the motility of the stomach or the secretion of gastric juice. H. W. D.

**Thjøtta, T.**, and **Avery, O. T. Growth accessory substances in the nutrition of bacteria.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **18**, 197.

Thjøtta has shown that *B. influenzae* will grow in blood-free broth containing the mucoid material from cultures of Friedländer's bacillus, and allied organisms.

The observations have been extended, and it is found that filtered extracts of yeast, vegetables (tomatoes, green peas, and string beans) are also efficacious in stimulating growth. The amount of extract necessary is 1–1,000. Growth, however, does not take place continuously in these media. There are two factors necessary for continuous growth. One is the substance, or group of substances, which are furnished by yeast or vegetables, which is resistant to boiling for ten minutes, but which is destroyed by autoclaving. It passes unchanged through a Berkefeld filter. The agent is obviously of a vitamine nature, and is called the V factor. The second factor is called X and is yielded by blood which contains both substances. The X factor is more resistant to heat, and autoclaved blood media may be reactivated by the addition of the V factor. One of the interesting points brought out is the early profuse growth of the bacteria in media supplied with both factors. C. G. L. W.

**Neuberg, C., Nord, F. F., u. Wolff, E.** Acetaldehyde als Zwischenstufe bei der Vergärung von Zucker durch *B. lactis aerogenes.* [**Acetaldehyde as the intermediary substance in the fermentation of sugar by *B. lactis aerogenes.***] *Biochem. Ztschr.*, 1920, **112**, 144.

**Cohen, C.** Über die Bildung von Acetaldehyde bei den Umsetzungen von Zucker durch Pilze. [**On the formation of acetaldehyde during the decomposition of sugar by moulds.**] *Biochem. Ztschr.*, 1920, **112**, 139.

The recent work of Neuberg and others is tending to emphasize the importance of acetaldehyde ($CH_3CHO$) as the central link in carbohydrate metabolism. There are further some grounds for a belief that in the higher organism the breakdown of sugar follows in the main the same course as that of the yeast cell. In these papers it is shown that acetaldehyde can be separated during sugar fermentation by moulds such as *Aspergillus niger*, and also by the *Bacillus lactis aerogenes.* Thereby our views on the general importance of acetaldehyde in carbohydrate metabolism are further strengthened. R. A. P.

**Hahn, M., u. Skramlik, E.** Versuche mit Antigenen und Antikörpern an der überlebenden, künstlich durchströmenden Leber. II. Versuche mit Tetanustoxin. [**Experiments with antigens and antibodies upon the surviving, artificially perfused liver. Tetanus toxin.**] *Biochem. Ztschr.*, 1920, **112**, 151.

The authors have shown that tetanolysin has a great affinity for liver tissue. In the perfusion of it through the liver, it is combined in such a way that it cannot be removed by vigorous perfusion with the antitoxin. It requires a relatively large amount of toxin in antitoxin-toxin mixtures to prevent such removal by the liver cells. This throws light upon the old observation that only large doses of antitoxin are able to make the poison ineffective in the body. When combined the lysin can affect other body cells; for instance, red blood corpuscles can be agglutinated by perfusion through such a liver. Tetanospasmin is not combined by liver tissue in any significant amounts. This selective combination confirms again the two-component nature of tetanus toxin, found by Ehrlich and Madsen. The tetanus toxin in these experiments was prepared for mice. For the haemolytic effect, rabbit's and guinea-pigs' corpuscles were used. The liver was that of the guinea-pig. R. A. P.

## RADIOLOGY

### *Radioscopy*

**Palugyay, J.** Röntgenologische Beobachtungen über die Anatomie und Physiologie der Kardia. [**Röntgen observations on the anatomy and physiology of the cardia.**] *Arch. f. d. ges. Physiol.*, 1921, **187**, 233.

Owing to the relations of the cardia, it is by no means easy to obtain a good view by X-ray methods when patients are in any normal positions. But a good view of the cardia and of the lower part of the oesophagus can be obtained in patients lying on the back with the pelvis raised so that the body has an inclination of 45° with the horizontal. The rays are passed postero-anteriorly, and an ordinary screen used. A further advantage of the posture is that the passage of food through the sphincter is so slowed down that its progress may be observed. The form of the stomach, the position of the cardia, and the passage of food along the oesophagus and into the stomach, as deduced from observations on 100 patients, are described. The cardia appears never to remain open, even in the empty stomach, but only to open for a brief interval to allow food which awaits admittance to pass into the stomach. As the stomach fills up, small peristaltic waves can be seen passing from the cardia along the greater curvature.

C. L. E.

### *Radio-diagnosis*

**Osgood, H. A. X-ray interpretation of the gastro-intestinal tract.** *Am. J. Electrotherap. & Radiol.*, 1921, **39**, 17.

The author stated there are three main sources of approach: (1) history; (2) laboratory findings; (3) X-rays; of these the history is the most important. Recently X-rays have come to the front: although negative results cannot exclude such lesions as a small peptic ulcer, positive findings are fairly conclusive, especially in surgical types of cases. X-ray will save time and prevent malignant cases becoming inoperable and is relatively inexpensive. Examination should combine the fluoroscope with a series of X-ray plates of the whole gastro-intestinal tract, not the stomach alone. The same type of barium meal should always be used. The author then gave a short differential diagnosis of the commoner lesions occurring in the various portions of the gastro-intestinal tract. In conclusion, he stated that the X-ray findings must not be relied upon alone for a diagnosis, and if needs be should be repeated.

P. L.-B.

**Gourbis.** Le syndrome atonique des voies digestives chez les nerveux. Étude de radiologie clinique. [**The atonic syndrome of the digestive tract in nervous persons. A study in clinical radiology.**] *Thèses de Lyon*, 1920, 82. (*J. de radiol. et d'électrol.*, 1921, **5**, 88.)

Attention has been drawn by different papers on radiology to the atony of various segments of the digestive tract. The author sets forth some radiological researches taking in every branch of the digestive tract systematically. It is from the oesophagus that the most characteristic signs are seen. Solids, shown under the screen by a cachet of bismuth, do not pass down with a continuous movement but by jerks, 'by steps'. The stoppages are more or less numerous and of long duration; some small very limited oscillating movements can be seen, but there is never any antiperistalsis as in stenosis. With semi-solids and also sometimes with liquids, particles can be seen which adhere to the atonic wall until the swallowing of a mouthful of water sweeps them away. At the level of the stomach one can usually verify some degree of ptosis, distension, and above all decrease in peristalsis, from which, in many cases, retention results. In the intestine the passage of the contrast mass usually appears normal, but some ptosis of the large intestine and an excessive stasis of the bismuth in the caecum and colon is found. This atonic syndrome, sometimes localized and sometimes generalized, needs looking into. It does not correspond to any organic lesion of the digestive tract, but its association with nervous manifestations makes it important and gives it interest. Most often, indeed, the patients in whom it is observed are nervous, emotional, neurasthenic, or hysterical. From that arises a point of practical importance: when persistent gastric or intestinal manifestations are of the nature to make one think of an organic lesion (ulcer, appendicitis, &c.), the co-existence of the atonic syndrome and signs of neuropathy will be a serious argument in favour of a nervous origin of the symptoms and will demand withholding surgical measures.

In conclusion, we can only advise the perusal of this study of clinical radiology suggested by Barjon: it is equally interesting for the practitioner and the specialist. P. L.-B.

## *Radiotherapy*

**STRAUSS, O.** Sur la radiothérapie de la polycythémie. [**The radiotherapy of polycythaemia.**] *J. de radiol. et d'électrol.*, 1921, **5**, 92.

The efficiency of radiotherapy in polycythaemia is dependent upon the influence that the X-rays exert upon the haematopoietic system. Experience has shown that irradiation of the spleen is not sufficient: it is necessary to irradiate the whole of the skeleton, the bone marrow in a functional hyperactivity appearing particularly radio-sensitive. Radiation of the long bones is the most easily carried out, but it is not sufficient to stop there; the sternum, pelvis, vertebral column, and scapula ought to be treated also. The author does not consider himself able, from his own experience, to speak of knowing how far it would be of advantage to combine irradiation of the spleen with X-radiation of the skeleton. To elucidate this point it would be necessary to make a series of observations in which the treatment would be carried out sometimes with and sometimes without irradiation of the spleen. There is no need to concern ourselves with the liver, as hypertrophy of this organ in polycythaemia is due entirely to hyperaemia.

P. L.-B.

**BÉCLÈRE.** La radiothérapie dans la maladie de Basedow. [**The use of radiotherapy in Basedow's disease.**] *J. méd. franç.*, 1920, **9**. (*Arch. d'électric. méd.*, 1920, **28**, 348.)

Radiotherapy is the ideal treatment for Basedow's disease and for all forms of hyperthyroidism, for, better than intervention, it destroys the secreting elements, or, at any rate, diminishes their secretory activity. When the morbid condition does not date back more than a year and the gland is soft, treatment by intensive doses at long intervals only takes from two to three months. In chronic forms, with a hard gland to which are added hyperplastic lesions of the connective tissues, the treatment takes at least six months, and improvement remains incomplete. In simple hyperthyroidism, on the contrary, radiotherapy is always perfectly successful, but it is in serious forms with extreme wasting and intense rapidity of heart-action that this method gives the best results.

Irradiation should be penetrating (20 cm. equivalent spark gap, 5 mm. aluminium, 20 cm. distance from the anticathode, localizing cylinder 10 cm. in diameter), séances should be weekly, and the dose 3 H.

Radiotherapy should be directed towards the function and not towards the lesion, and should be guided by the disorders of circulation (frequency and inequality of the heart-beats) and avoid substituting for excess a deficiency of the thyroid secretion. S. U. L.-B.

**McCaskey, D.** **Quartz ultra-violet therapy and kinetic energy.** [*N. York M. J.* (&c.), 1919, **110**, 1058. (*J. de radiol. et d'électrol.*, 1920, **4**, 429.)]

Under the influence of ultra-violet rays the oxidations of the organism are greatly increased: each time the author used this treatment for diabetes mellitus he noted that the patient showed signs of intoxication similar to anaphylactic shock. Nevertheless, he considers that, of the whole arsenal of medicine at the present time, this treatment is the surest and most efficacious means of successfully combating the uric acid diathesis, neurasthenia, chlorosis, asthma, influenza, pneumonia, chronic ulcer of the leg, and, in general, all manifestations of diminished vitality.

The progress of the patient should be closely followed; a complete analysis of urine should be made, with comparison between uric acid nitrogen and total nitrogen. The patient must be weighed, his arterial tension taken, and an electro-cardiogram made; chemical analysis of the blood should be made as well as measurement of the diameter of corpuscles, and all these results should be compared from time to time with new analyses.

S. U. L.-B.

**Lenormant, C.** Sclérose diffuse de la peau et du tissu cellulaire du cou consécutive à un traitement radiothérapique prolongé : torticolis cicatriciel, œdème éléphantiasique de la face, compression laryngo-trachéale. [**Diffuse sclerosis of the skin and of the cellular tissue of the neck following prolonged radiotherapy: cicatricial torticollis, marked oedema of the face, laryngo-tracheal compression.**] *Bull. et mém. Soc. de chir. de Par.*, 1920, October 27. (*Arch. d'électric. méd.*, 1920, **28**, 366.)

The author showed a child of 15 years who underwent radiological treatment every other day for seven months for a bacillary adenitis of the neck. During treatment an ulcerative radio-dermatitis came on ; this healed during a stay at Berck, but the patient's head and neck then presented a kind of sclerosed retractile mass, from one ear to the other, affecting the submaxillary region and the anterior part of the neck. The head was drawn towards the left shoulder ; the acromial end of the clavicle was subluxated upwards ; there was great oedema of the right side of the face, and symptoms of laryngo-tracheal compression. The sclerosed retractile tissue formed a band which gradually strangled the patient. P. L.-B.

**Bergonié, J.** Thermodermite consécutive à une radiodermite chronique. [**Heat dermatitis following a chronic X-ray dermatitis.**] *Arch. d'électric. méd.*, 1920, **28**, 353.

The author states that various physical agents have an ill effect on the site of an old X-ray dermatitis because of the devitalized condition of the part. Records of a case are given in which a chronic X-ray dermatitis followed treatment for a uterine fibroid; although this healed, the site very easily became irritated or ulcerated from mechanical irritation such as heat, cold, or friction. P. L.-B.

### *Radium Therapy*

**Beuttner, O.**, et **Chapuis, R.** *La curiethérapie du cancer du col de l'utérus.* [**The radium therapy of cancer of the cervix.**] Geneva, edition Atar, 1921, pp. 26, &c.

The author summarizes the results of radium therapy in cases of cancer of the cervix which have been under treatment at the Swiss Radium Institute in Geneva from 1914–18. For descriptive purposes the 63 cases under review are classified in four groups, according to the condition and its degree of operability. An inspection of the data in Tables I–IV will show that the best results are obtained in those cases in which the disease is least advanced.

The author lays great stress upon the care which is bestowed upon every aspect of the therapy; the details of clinical history and the state of health of the patient are very carefully inquired into. The technique of administration of the radium follows well-recognized lines and consists for the most part in the introduction of platinum tubes containing the radium into the cervical canal, such radiation being supplemented by plaques. The publication is one which will repay study, for, though no new ground is broken, the work is replete with clinical detail, indicative of carefully-planned effort.

*Group I.* The first group includes cases of operable cancer of the cervix, the growth being restricted to definite limits.

A. Five patients are dead, viz.:

| Case. | First Application of Radium. | Date of Death. | Duration of Survival. |
|---|---|---|---|
| 1 | 19.v.1914 | 26.ix.1915 | 16 months |
| 2 | 30.xii.1914 | 8.ii.1916 | 13 ,, |
| 3 | 11.vii.1916 | 16.i.1917 | 6 ,, |
| 4 | 11.v.1915 | 26.i.1919 | 44 ,, |
| 8 | 22.ix.1917 | 6.i.1919 | 16 ,, |

B. Four patients are alive, viz.:

| Case. | First Application of Radium. | Last Condition. | Duration of Recovery. |
|---|---|---|---|
| 5 | 12.xii.1914 | 24 iii.1920 | 63½ months |
| 6 | 13.ix.1915 | 5.iii.1920 | 54½ ,, |
| 7 | 14.vi.1917 | 15.iii.1920 | 33½ ,, |
| 9 | 17.ix.1917 | 14.viii.1918 | 26½ ,, |

In the Group A the shortest duration of survival is 6 months, and the longest 44 months.

In the Group B, the shortest duration of recovery (clinical) at the time of the last report is 26½ months, and the longest 63½ months.

*Group II.* The second group includes cases of cancers far advanced.

A. Four patients are dead, viz.:

| Case. | First Application of Radium. | Date of Death. | Duration of Survival. |
|---|---|---|---|
| 1 | 6.xii.1916 | 11.xi.1917 | 11 months |
| 2 | 22.v.1917 | 29.viii.1918 | 15 ,, |
| 3 | 14.viii.1917 | End x.1918 | 14½ ,, |
| 4 | 15.iii.1915 | 4.iv.1920 | 60½ ,, |

B. Four patients are alive, viz.:

| Case. | First Application of Radium. | Last Condition (or Latest Report). | Duration of Recovery (Clinical). |
|---|---|---|---|
| 5 | 26.iv.1915 | 20.iv.1920 | 60 months |
| 6 | 12.viii.1915 | 3.iii.1920 | 54½ ,, |
| 7 | 27.v.1916 | 16.iv.1920 | 46½ ,, |
| 8 | 30 xi.1916 | 18.viii.1920 | 44½ ,, |

In Group A the shortest duration of survival is 11 months and the longest 60½.

In Group B the shortest duration of recovery (clinical), at the time of the last report, is 44½ months, and the longest 60 months.

*Group III.* The third group includes cases of cancer which were definitely inoperable, the uterus, however, retaining some degree of mobility.

A. 18 patients are dead, viz.:

| Case. | First Application of Radium. | Date of Death. | Duration of Survival. |
|---|---|---|---|
| 1 | 13.iii.1916 | 9.ix.1916 | 6 months |
| 2 | 22.v.1914 | 6.i.1915 | 7½ ,, |
| 3 | 6.ii.1915 | 21.xii.1915 | 10 ,, |
| 4 | 15.v.1914 | 4.iv.1915 | 11 ,, |
| 5 | 25.v.1915 | 4.iv.1916 | 10 ,, |
| 6 | 8.v.1915 | 2.vi.1916 | 13 ,, |
| 7 | 15.ii.1915 | 29.vii.1916 | 17½ ,, |
| 8 | 29.iii.1916 | 17.xii.1917 | 20½ ,, |
| 9 | 13.iv.1916 | 5.v.1918 | 24½ ,, |
| 10 | 22.ix.1911 | 1.ii.1916 | 29 ,, |
| 11 | 23.vii.1915 | 16.viii.1917 | 24½ ,, |
| 12 | 30.vii.1915 | 21.iv.1918 | 32½ ,, |
| 13 | 20.iii.1914 | 25.i.1917 | 34 ,, |
| 14 | 17.ii.1915 | 26.vii.1918 | 41½ ,, |
| 20 | 20.i.1917 | 27.vii.1919 | 30 ,, |
| 21 | 3.ix.1917 | 14.xi.1918 | 12½ ,, |
| 23 | 14.x.1916 | 17.xi.1918 | 25 ,, |
| 25 | 16.iv.1917 | 1.ix.1918 | 16½ ,, |

B. Seven patients are alive, viz.:

| Case. | First Application of Radium. | Last Condition. | Duration of Recovery (Clinical). |
|---|---|---|---|
| 15 | 25.ii.1916 | 13.iv.1920 | 49½ months |
| 16 | 2.iv.1916 | 28 v.1920 | 50 ,, |
| 17 | 3.vi.1916 | 9.iv.1920 | 46 ,, |
| 18 | 25.vii.1916 | 10.v.1920 | 45 ,, |
| 19 | 9.xii.1916 | 10.ii.1920 | 38 ,, |
| 22 | 7.ix.1916 | 18.ii.1920 | 41 ,, |
| 24 | 11.x.1916 | 4.iv.1920 | 41½ ,,<br>(only one application) |

In Group A the shortest duration of survival is 6 months and the longest 41½ months.

In Group B the shortest duration of recovery (clinical), at the time of the last report, is 38 months and the longest 50 months.

*Group IV.* The fourth group includes very advanced cases, the patients often being in a cachectic condition.

A. 18 patients are dead, viz.:

| Case. | First Application of Radium. | Date of Death. | Duration of Survival. |
|---|---|---|---|
| 1 | 16.vii.1915 | 1.xi.1915 | 3½ months |
| 2 | 20.vii.1916 | 6.i.1917 | 5½ ,, |
| 3 | 15.vii.1914 | 31.xii.1914 | 5½ ,, |
| 4 | 12 v 1914 | ? xi 1914 | 6 ,, |
| 5 | 5.i.1917 | 2.vi.1947 | 5 ,, |
| 6 | 2.xi.1914 | 14.vi.1915 | 7½ ,, |
| 7 | 12.vii.1915 | 2.iii.1916 | 7½ ,, |
| 8 | 12.vi.1917 | 14.ii.1918 | 8 ,, |
| 9 | 10.vi.1914 | 15.vi.1915 | 12 ,, |
| 10 | 18.vii.1914 | 22.vi.1915 | 11 ,, |
| 11 | 30.v.1915 | 4.iv.1916 | 10 ,, |
| 12 | 23.x.1915 | 20.viii.1916 | 10 ,, |
| 13 | 24.iii.1915 | 1.vi.1916 | 14 ,, |
| 14 | 12.iv.1915 | 23.vii.1916 | 15 ,, |
| 15 | 29.iv.1915 | 23.vii.1917 | 26½ ,, |
| 16 | 18.iii.1914 | 20.i.1916 | 22 ,, |
| 17 | 4.v.1916 | 5.iii.1918 | 23 ,, |
| 18 | 1.iii.1916 | 8.ii.1918 | 23 ,, |

B. One patient is alive, viz.:

| Case. | First Application of Radium. | Last Condition. | Duration of Recovery (Clinical). |
|---|---|---|---|
| 19 | 20.vi.1917 | 24.xi.1920 | 41 months |

C. Two patients are unrecorded, viz.:

| Case. | First Application of Radium. | Last Condition. | Number of Applications. |
|---|---|---|---|
| 20 | 9.vi.1915 | End ix.1915 | 4 |
| 21 | 6.vii.1914 | 22.vii.1914 | 2 |

In Group A the shortest duration of survival is $3\frac{1}{2}$ months and the longest $26\frac{1}{2}$ months.

In Group B one single patient, whose first application dated June 20, 1917, was suspected to have a recurrence about 41 months later.

S. R.

**Barclay, A. E. A danger of the Coolidge tube for screen work.** *Arch. Radiol. & Electroth.*, 1921, **25**, 225.

In working with a Coolidge tube it is difficult to protect the observer from undesired radiation. In several plates, whatever the size of the diaphragm, there was always an enlarged reproduction of the anticathode in proportion to the size of the opening in the diaphragm. The production of the image is due to radiations from the anticathode. From the practical point of view, recognition of this secondary radiation is of great importance when using the upright stand. The danger can be prevented by turning the tube upside down with the anticathode below, so that its image goes upward above the primary X-ray shadow. P. L.-B.

### *Radiobiology*

**Weinberg, J. A.** Influence de l'exposition aux rayons X sur l'évolution de la tuberculose. [**The influence of exposure to X-rays on the growth of tubercalosis.**] *Schweiz. med. Wchnschr.*, 1920, **1**, No. 14. (*J. de radiol. et d'électrol.*, 1921, **5**, 92.)

Weinberg intended in the first place to find out whether irradiation by X-rays is capable of accelerating the development of human tuberculosis in the guinea-pig, in the second place to determine the rôle of the lymphocytes in combating a tuberculous infection in that animal. He submitted guinea-pigs to massive doses of rays and inoculated them on the following day intraperitoneally with cultures of human tubercle bacilli. In two series of animals treated thus, in which the duration of irradiation alone varied, he did not establish any appreciable difference in the time of appearance of the disease in the irradiated animals and in the controls. In a third series, in which a second irradiation was made some days after the inoculation, death occurred nearly at the same date as in the controls, two days earlier on the average. The result was the same in a fourth series, in which the two irradiations were made before the inoculation. Histological and post-mortem examination did not show any marked difference in degree between the lesions in the irradiated animals and in the controls.

Exposure to X-rays, however, has a very marked effect on the metabolism of the animal, shown by a loss of weight more rapid than in the controls, and impossible to ascribe to an acute development of tuberculosis. The leucocytes, and particularly the lymphocytes, show marked modifications: great diminution in the number of white cells and of the percentage of lymphocytes, the more marked the longer the irradiation. In sections of the liver and spleen the vessels show far fewer polymorphonuclears and lymphocytes in the irradiated animals than in the controls, and the same difference is found in the peripheral zone of the tubercles, where the lymphocytes are few in numbers. On the other hand, the epithelioid cells and large mononuclears are normal in numbers, so that it can be inferred that these cells do not originate from lymphocytes, as Metchnikoff taught. The presence of a large number of leucocytes in and around the vessels near the tubercles in the controls indicates that these cells are brought to the lesions by the blood and are not the result of tissue reaction. P. L.-B.

**Pech.** Phénomènes d'antagonisme entre diverses radiations (ultra-violet, spectre visible, infra-rouge). [**Phenomena of antagonism between different rays (ultra-violet, visible spectrum, infra-red).** *Compt. rend. Acad. d. sc.*, 1920, **170**, 1246. (*J. de radiol. et d'électrol.*, 1920, **4**, 429.)

It is known that certain effects obtained by beams rich in ultra-violet light on a physico-chemical equilibrium are diminished if the proportion of red or infra-red is augmented without changing the intensity of the ultra-violet. The author adds to the interest of this law by some noteworthy experiments.

1. Raw cotton becomes bleached when exposed to the rays of the mercury arc through a quartz window. When solar rays, ordinary electric rays, infra-red or visible rays in general are added, the bleaching process becomes slower or stops.

2. The same mercury-vapour lamp produces, under certain conditions in a dark room, a cutaneous erythema in five minutes. If to this be added infra-red or a sufficiently powerful light, it takes seven minutes. It is difficult to prove the antagonism with sensitized papers and photographic plates. Fluorescent effects on the sulphides produced by the ultra-violet rays only obtain with wave-lengths greater than the orange; shorter wave-lengths are reinforced. From these facts the author draws the following conclusion: in a bundle of radiations capable of producing modifications in a given physico-chemical equilibrium there exists, in certain cases, a bundle of other radiations which, if added to the former, without introduction of any other change in the conditions, oppose the development of the modifications. The characteristics of the antagonizing bundle seem to depend, not only on those of the active bundle, but also on the nature of the physico-chemical equilibrium to be modified. S. U. L.-B.

**Le Bon, G.** Sur certaines propriétés antagonistes des diverses régions du spectre. [**Certain antagonistic properties in different regions of the spectrum.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1450. (*J. de radiol. et d'électrol.*, 1920, **4**, 429.)

In connexion with the article by Pech (abstracted above), the author states that he has already pointed out the antagonism between different radiations on phosphorescent bodies and on vegetables. The infra-red destroys the green matter in plants.

Transformation of the infra-red into visible light may be effected by using phenomena of the same nature. S. U. L.-B.

# MEDICAL SCIENCE

## ABSTRACTS & REVIEWS

VOLUME IV. NUMBER 5 AUGUST 1921

## CONTENTS

REVIEWS:

PAGE

DYSENTERY . . . . . . . . . . . . . . 399

CONGENITAL SYPHILIS . . . . . . . . . . . 406

STATISTICS RELATING TO THE TREATMENT OF CANCER OF THE BREAST BY EXCISION SUPPLEMENTED BY RADIATION . . 418

THE POST-MORTEM EXAMINATION OF A CASE OF ARTERIO-VENOUS ANEURYSM BETWEEN THE INTERNAL CAROTID ARTERY AND THE CAVERNOUS SINUS . . . . . . . . . . 424

THE RÔLE OF ANOXAEMIA IN THE PRODUCTION OF SYMPTOMS IN DISEASE AND INJURY OF THE NERVOUS SYSTEM . . 427

ABSTRACTS:

SURGERY . . . . . . . . . . . . . . . 435

NEUROLOGY . . . . . . . . . . . . . . 441

PATHOLOGY AND BACTERIOLOGY . . . . . . . . . 450

BIOCHEMISTRY . . . . . . . . . . . . . 468

RADIOLOGY AND ELECTROLOGY . . . . . . . . . 481

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## NOTICE.

*In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.*

# REVIEWS

## DYSENTERY

**Historical.** According, to Bonnet and Sicard the term 'emerods' mentioned in the Bible (1 Samuel, chaps. v and vi) applies to the prolapse of the rectal mucous membrane occurring in epidemic dysentery in the tropics. In support of this view they allude to the frequency of prolapse of the rectal mucous membrane in epidemic dysentery in hot countries, the absence of epidemicity in haemorrhoids, and the clinical description of dysentery as given in the Vulgate.

**Epidemiology.** Stokes and Bigger give a short account of an epidemic of dysentery in Dublin in the autumn of 1919, which is of interest historically as there has been no other outbreak of dysentery in Dublin in modern times. Of 186 cases notified 19 died, a mortality of about 10 per cent. At ages up to 45 years the mortality was 3·8 per cent., and from 45 upwards 43·3 per cent. The areas from which most of the cases came were very insanitary: tenement houses, overcrowding, and flies giving ample scope for the spread of an epidemic. The Shiga bacillus was isolated in 101 cases and an organism of the Flexner group in one case only.

Vallardi describes the epidemic of bacillary dysentery observed in Macedonia during the summer of 1918. The Shiga bacillus was found in 79·06 per cent., the Flexner bacillus in 20·35 per cent., and the Y bacillus in 0·58 per cent. The mortality was relatively low, being only 0·8 per cent. among the Italian troops, and 3·5 per cent. among the Allied troops in a total of 5,000 cases from May to October 1918.

Jennicke reports an outbreak of 108 cases of Shiga bacillus dysentery with 19 deaths at Kittelsthal, a small village in the Thüringen forest. He attributes the epidemic to 'carriers' who had returned from imprisonment in France.

Cases of dysenteriform catarrh of the large intestine due to flagellata were observed by Grothusen in German East Africa. The condition, of which he has found no description in the literature, was curable by thymol followed by calomel.

**Aetiology.** Paraf made the following observations in a hospital containing patients with bacillary dysentery where flies were very prevalent: (1) Flies swarming round the dejecta of dysentery patients were frequently found to be carriers of the Shiga bacillus. (2) The Shiga bacillus was found in the bodies of flies caught in wards in which cases of dysentery had occurred. (3) The dysentery bacillus was found in food exposed to the air in surgical wards in which there were swarms of flies. (4) As regards the mode of transmission, cultures of flies' legs and wings were positive in only

2 out of 16 cases, whereas cultures of the alimentary canal were positive in 11 out of 24 cases. (5) The maximum duration of the survival of the dysentery bacillus in the fly's intestine was found to be five days. After that date the cultures were negative.

**Dysentery in children.** According to Davison over 80 per cent. of the acute cases of ileocolitis, both in Baltimore and in Birmingham, Alabama, were due to infection with *B. dysenteriae.* Flexner's bacillus was more prevalent than Shiga's bacillus in Baltimore, Maryland, and Birmingham. Clinically as well as bacteriologically the Baltimore and Birmingham cases were identical. *B. dysenteriae* (either Flexner or Shiga) was not found in the stools of 63 cases of simple diarrhoea nor in those of 100 normal children. Davison urges that the name 'ileocolitis' should be changed to 'dysentery' in children and that the disease should be made notifiable. He is of opinion that dysentery is spread from the stools of the patient to the food and mouths of other children by flies and infected hands, and not disseminated from a general dairy source. The disease is least prevalent among children receiving breast milk, boiled milk, and boiled milk mixtures in boiled vessels.

As illustrating the predilection of dysentery for children, Vogt, of Magdeburg, alludes to the epidemic at Barmen in 1899–1901, in which 899 adults were affected and 560 children, the mortality among children being 6·3 per cent. as compared with 4·6 per cent. among adults. Recent observations by Hotzen have shown that the dysentery cases in the hot summer of 1917 amounted to 69 per cent., or nearly two-thirds of all the cases of acute disturbance of nutrition in infants. Of 123 cases in which the diagnosis of dysentery was established bacteriologically 55 or 44 per cent. succumbed, and, even if only those cases be considered in which other diseases than dysentery could be excluded, the mortality was still 23 per cent. Vogt concludes that the significance of dysenteric infection in infancy has formerly been underestimated, and that a considerable proportion of the acute intestinal diseases observed during the hot season were really due to dysentery.

Jacki reports an epidemic of Shiga bacillus dysentery in the Heidelberg Children's Clinic. The total number of cases was 102, of whom 57 were under 1 year. The duration of the fatal cases ranged from 4–23 days. The post-mortem examination showed typical dysenteric lesions of the catarrhal, diphtheritic, and ulcerative forms. The source of infection was probably two nurses who were engaged in washing out the milk bottles and whose blood in a dilution of 1 in 200 caused agglutination of Shiga bacilli. One gave a history of intestinal catarrh a year previously and the other could not remember any intestinal attack.

Young reports an isolated case of amoebic dysentery which occurred in a London children's hospital in a boy aged 3. The father had never been out of England and no source of infection could be established. Rapid recovery followed treatment by hypodermic injections of emetine hydrochloride.

**Symptomatology.** Manson-Bahr states that monarthritis, or more generally polyarthritis, was frequently noted during the Egyptian and Palestine campaigns as a complication of bacillary dysentery. In amoebic dysentery, on the other hand, arthritis appears to be very rare, Manson-Bahr having found a record of only one case. During the first nine months of 1916 a number of cases of arthritis occurred among patients suffering from bacillary dysentery in Egypt. The bacillus responsible was the Shiga bacillus in all the cases which could be properly investigated, and no examples of arthritis were observed in Flexner-Y infections. The majority of the cases occurred in patients who had been treated with antidysenteric serum, though twice it was met with in cases untreated by serum of any kind. Manson-Bahr classifies the cases of arthritis occurring subsequent to the administration of antidysenteric serum under two headings: (*a*) fugitive polyarthritis with or without joint effusions, occurring during the course of serum sickness; (*b*) intractable polyarthritis with effusion into joints and wasting of adjacent muscles apparently due to absorption of dysenteric toxins. In two cases previous arthritis of rheumatic or traumatic origin had occurred a year or more before the onset of dysentery, so that it is probable that previous joint injury exercises a very definite predisposing influence on the supervention of joint symptoms in a subject subsequently attacked by bacillary dysentery.

In Manson-Bahr's series a polyarthritis occurred in 8 out of 29 injected with a certain brand of serum, whereas there was only one example of arthritis among 335 convalescent and slight bacillary cases admitted to hospital during the same period and who were not treated with serum of any kind.

In a paper based on 33 cases of dysenteric arthritis seen at Malta, Graham states that the usual day of onset was between the sixth and twenty-third day after the first symptoms of dysentery. There was no relationship between the time of onset of the arthritis and the severity of the dysentery. The first symptom was severe pain, which preceded the swelling of the joint by some hours. The effusion into the joint took place quickly and was usually very large. In severe cases there was a considerable rise of temperature which might oscillate for several weeks. In mild cases the temperature was little if at all raised. When the arthritis subsided quickly there was seldom any after-trouble, but when the process was a slow one with relapses there was often stiffness. Some of the patients developed eye symptoms which were of two kinds: (1) infection of the conjunctiva without purulent discharge but with pain and lacrymation; (2) cyclitis or irido-cyclitis. According to Graham the joint affection runs a slow course, but apparently ends in complete recovery.

Glaessner examined the gastric and pancreatic secretions in cases of acute and chronic bacillary dysentery with the following results: In four acute cases the gastric juice though containing hydrochloric acid showed a definite subacidity, and the trypsin was decidedly diminished. In one out of four chronic cases achylia gastrica was found with very low total acidity, and trypsin had almost completely disappeared. Glaessner thinks that the relative pancreas achylia in acute dysentery and the complete pancreas achylia in chronic dysentery is of value in the diagnosis, prognosis, and treatment of the disease. The prognosis is decidedly more unfavourable in cases with pancreatic achylia than in others, and the deficiency of the pancreatic secretion should be taken into account in treatment.

Albu regards the chronic relapsing disease of the intestine and rectum after an attack of dysentery as so exactly like the condition formerly called ulcerative colitis that he has come to the conclusion that the latter is merely a sequel of bacillary dysentery. The objection that none of the dysentery bacilli have been found in ulcerative colitis no longer holds good, as this has been shown to be due to defective technique. Albu emphasizes the fact that there is not only a chronic but also an acute dysentery without any blood in the stools. Haemorrhage, he points out, is always a sign of ulceration of the mucous membrane, but by no means all cases of dysentery reach this stage. In mild cases there is not more than a marked hyperaemia and catarrhal swelling of the mucous membrane, which leads to increased secretion of mucus and water but not to haemorrhage.

Rey records a fatal case of dysentery in a woman aged 36, caused by Morgan's No. 1 or No. 14 bacillus. The autopsy showed that the portion of bowel involved extended from the hepatic flexure to the splenic flexure, the transverse colon showing a multitude of large and small ulcers eating through the muscular coats and adhering to the omentum. No actual perforation had occurred.

Lemann reports a case in a woman, aged 48, of Shiga bacillus dysentery following the eating of a cream puff, with pseudo-membrane in the vagina and oedema of the abdominal wall. Shiga bacilli were obtained from cultures from the vaginal pseudo-membrane and from the cervix. The membrane in the vagina corresponded exactly to that occurring in the bowel of dysentery patients, showing that the bacilli seem to act on the vaginal as they do on the intestinal mucous membrane. The contamination of the vagina was probably due to the recent discharge, especially as the inflammation was most extensive and intense at the introitus. No explanation could be given of the oedema of the abdominal wall.

Moorhead records a fatal case of myelitis in a man, aged 55, suffering from Shiga bacillus dysentery and marked arthritis of both knee-joints. The autopsy showed typical meningo-myelitis an inch in extent, in the centre of the lumbar swelling.

According to Buttenwieser, of the Frankfort University Medical Clinic, haemorrhagic encephalitis is a very rare complication of dysentery, especially in adults, though he believes that, if a careful clinical and anatomical examination of the brain were made, encephalitis would be oftener found in dysentery like that present in other infectious diseases. He records a fatal case in a woman aged 49, in whom the symptoms were those of lethargic encephalitis. The possibility of there being an accidental association of dysentery and influenzal encephalitis was excluded by the epidemic form of influenzal encephalitis having subsided for several months. Lenhartz's case of encephalitis in dysentery also occurred at a time (1880) when influenza was not prevalent.

An extremely acute case of amoebic dysentery is reported by Vaccarezza and Finochietto. The patient was a man, aged 30, who suddenly developed symptoms of colitis and proctitis, followed in the course of the next fortnight by evidence of peritonitis, which was chiefly localized in the right iliac fossa. Death took place on the twentieth day of disease from necrosis of the caecum and terminal portion of the ileum, in which a large perforation was found. Numerous amoebae were found in the intestinal ulcers and gangrenous tissue.

According to Hornus, amoebic dysentery is very prevalent in Morocco, where, in addition to the acute and typical forms, there exist larval unrecognized ones which are manifested only by the hepatic complications. He records a case which was atypical enough to be mistaken for pulmonary tuberculosis, and it was only by examination of the pus expectorated from a hepatic abscess that a diagnosis could be made.

Mallory reports a case of solitary abscess of the liver in a Canadian aged 53, which occurred 30 years after residence in Central America, where he had suffered from an attack which he described as diarrhoea, not dysentery. Recovery followed operation and treatment by emetine hydrochloride. Characteristic chocolate-coloured pus was found in the abscess, but no amoebae. Mallory's conclusions are as follows: (1) Amoebic dysentery, and therefore an abscess of the liver, may occur in persons who have never been in tropical or subtropical countries. (2) Amoebic dysentery occasionally occurs a great many years after a primary and single attack of amoebic dysentery. (3) An abscess of the liver should be remembered as a cause of obscure fever.

Proust and Ramond report the case of a large empyema in a man, aged 59, caused by rupture of an amoebic hepatic abscess into the pleural cavity and cured without operation by simple puncture and administration of emetine and novarsenobenzol.

Legrand records two cases of multiple abscesses which occurred in his practice at Alexandria in 1911 and 1913, i. e. before the introduction of emetine. The first patient was a man, aged 43, with a perinephritic abscess and abscesses in the sacrum, right thigh, and left shoulder, and the second patient was a man, aged 42, with amoebic abscesses in the right pleura, left lung, and left cerebellar hemisphere, although there was no clinical dysentery or hepatic abscess.

**Diagnosis.** Low records several examples, including syphilis, tuberculosis, malignant disease, ankylostomiasis, balantidiasis, and foreign bodies, as well as of schistosomiasis dysentery, paragonimus dysentery, and heterophyes dysentery to show that considerable care should be exercised in diagnosing cases presenting symptoms of dysentery. After careful examination of the stools he recommends that a rectal examination should be made either by the finger or sigmoidoscope.

**Prognosis.** Albu, who has had experience of several hundreds of cases of bacillary dysentery during the war, regards complete and permanent recovery from bacillary dysentery as an extremely rare event. Clinically a more or less marked irritability of the large intestine, and especially of the rectum, persists and on the slightest provocation gives rise to morbid symptoms. The anatomical cause for this irritability is a state of catarrhal inflammation of the mucous membrane.

**Treatment.** Pontano, whose previous paper on the diagnosis and treatment of hepatic abscess has recently been abstracted (vide *Medical Science*, 1920, **1**, 573), records ten illustrative cases to show that the fully developed amoebic hepatic abscess can be cured by specific medical treatment without operation. Emetine hydrochloride administered intramuscularly is, in his opinion, sufficient to arrest the necrotic process and cause more or less rapid absorption of the contents of the abscess. Medical treatment alone is indicated if the characteristic microscopical appearances are found, even in the presence of micro-organisms which can be cultivated from the pus. In such cases the micro-organisms do not usually possess any pathogenic properties but are ordinary saprophytes which are easily destroyed.

On the other hand, surgical treatment is indicated if the organisms show the capacity of transforming the necrotic product into true pus. Pontano does not regard the severity of the patient's condition, the size or duration of the abscess, as contraindications to medical treatment, which has a favourable action both on the co-existent dysentery and on multiple abscesses against which surgery is powerless. He concludes by saying that amoebic abscess of the liver should henceforth be regarded as a hepatic localization of amoebic dysentery and should come within the domain of medical treatment as much as the hepatic manifestations of syphilis.

Pontano's observations on the value of the medical treatment of hepatic abscess in dysentery are confirmed by Castigliola in a paper based on two years' experience at the military hospital at Bengasi, where amoebic dysentery is endemic, and also by Manini, who reports a case of hepatic abscess successfully treated by emetine without operation.

Panayotatou, of the Greek hospital at Alexandria, reports 34 cases of acute amoebic hepatitis, 6 of which were cured by emetine without operation, while the remaining 28, which were operated on after being treated by emetine for a week, presented large abscesses which had destroyed a considerable amount of the hepatic tissue. She maintains that though emetine is powerless in such cases it should always be employed for several days before an operation, as it prepares the soil, so to speak, for the operation, and may even render an operation unnecessary.

Legrand, who has been in practice in Egypt for 30 years, states that prior to the introduction of emetine he had to operate on 25–30 cases of hepatic abscesses a year, but that at present, owing to the employment of emetine, this figure has been reduced to 4 or 5, and the cases are less serious.

Foges, of Vienna, records 5 cases—4 in men and 1 in a woman—of severe rectal lesions following dysentery, in 4 of which the clinical picture resembled carcinoma of the rectum. Considerable improvement followed intrarectal treatment with the quartz lamp, but the end results could not be given as the patients were discharged from hospital at the end of the war.

Haughwout and Lantin report 8 cases of endamoebic dysentery and 1 case of bacillary dysentery treated with benzyl benzoate at the Philippine General Hospital. All the cases of amoebic dysentery were of the acute type and varied in severity. Markedly good results were obtained in every case. The benzyl benzoate was given in a small amount of cold water three times a day after food. The doses employed by Haughwout and Lantin varied from 20–30 drops of the 20 per cent. alcoholic solution, but in an addendum to their paper Asuzano records 2 cases in which equally good results were obtained by 10 drops only.

Korbsch and Gross, of Breslau, successfully treated six patients with chronic bacillary dysentery by intravenous injection of a vaccine composed of seven strains of the Shiga bacillus and one each of the Flexner and Y bacilli.

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J. D. R.

## CONGENITAL SYPHILIS

The important question of *antenatal syphilis,* and the inter-relationship between pregnancy and syphilis forms the subject of several recent articles. Hendry gives the results of his experience at antenatal clinics at Liverpool between 1916 and 1920. As the cases were all in the condition of latent syphilis, diagnosis depended upon the history of infection, the past obstetrical history, the Wassermann reaction, and examination of placenta and still-births. An analysis of the cases showed that the obstetrical history was not a reliable guide in any given case; that examination of still-births and placenta furnished reliable, but, very often, insufficiently available evidence; and that the diagnosis, therefore, had to depend chiefly on the Wassermann reaction, in spite of the fact that this reaction may be negative during pregnancy, and that a positive reaction may occur in a non-syphilitic individual. As the clinics were not adapted to arsenical treatment, mercury was employed in the treatment of the pregnant women, either in the form of grey oil injections or grey powder by the mouth.

The results are divided into three groups: (1) no treatment; (2) treatment during pregnancy; (3) under treatment when pregnancy began. In the first group of 43 cases there were 15 abortions, 17 still-births, 4 neonatal deaths, and 7 living infants. In the second group of 40 cases there were 2 abortions, 4 still-births, 5 neonatal deaths, and 29 living infants. In the third group of 11 cases all children were born alive. Hence mercurial treatment commenced before pregnancy justifies a favourable prognosis. When treatment is commenced during pregnancy Hendry remarks that the prognosis depends on the degree of infection of the foetus, which is an unknown quantity.

Williams (1) communicates a critical study of 302 *foetal deaths* occurring in 4,000 consecutive deliveries occurring between April 1916 and December 1919. In this series every effort was made to discover a history of syphilis and to detect signs of the disease. A Wassermann test was done on each patient, and if positive she was subjected to proper treatment. After delivery a Wassermann test was made from the foetal blood obtained from the maternal end of the umbilical cord. The placentas were examined histologically. Post-mortem examination of children born dead or who died after delivery was made whenever possible. Of the 302 dead infants 212 came to autopsy. In these, syphilis was found in 104, or 34 per cent. In 89 of these the diagnosis was confirmed by demonstration of spirochaetes in the foetal tissues, in the remainder from the presence of syphilitic lesions in the placenta and a positive Wassermann reaction in the mother. Syphilis was found to be the chief cause of death of the infants—34·4 per cent.—the other causes being dystocia, 15·2 per cent.; toxaemia, 11·5 per cent.; prematernity, 10·6 per cent.; placenta praevia, 5 per cent.; deformity, 3·6 per cent.; other causes, 10·6 per cent.; unknown causes, 8·6 per cent. Williams remarks that the 34 per cent. of proved syphilitic cases probably does not represent the true total of deaths attributable to syphilis, since in some of the cases classified as due to unknown causes the mothers gave a positive Wassermann reaction and there were syphilitic lesions in the placenta. This applies also to some of the deaths due to prematurity. Moreover, these figures do not include cases of congenital syphilis appearing in babies which were discharged alive, or in whom the disease developed later. It must be noted that more than half the cases were negroes, and it was found that the foetal mortality from syphilis was nearly four times greater among the negroes than the whites.

Concerning the results of treatment of the mothers, 421 cases which gave a positive Wassermann reaction are divided into three classes: (1) those who, for various causes, had no treatment; (2) those who had inefficient treatment consisting of two or three injections of '606' only; (3) those who had satisfactory treatment, consisting in 4 to 6 injections of '606', followed by a course of mercury, resulting in a negative Wassermann reaction. In these three categories there were 157, 103, and 163 patients respectively, and the results of treatment are shown by the fact that in the first group 52 per cent. of the children were born dead or showed signs of syphilis, as compared with 37 per cent. in the second group, and only 7·4 per cent. in the third group. Consequently, Williams concludes that in the future syphilis might be eradicated as a cause of foetal death in all properly conducted clinics in which the disease is recognized and properly treated prior to the middle of pregnancy.

The progressive *attenuation of the virulence of syphilitic infection in pregnant women* has long been known, and various explanations of this phenomenon have been suggested, one of the most recent being that of Routh, who attributes it to *spirillolysis* of the spirochaetes caused by the *chorionic ferments.* It has been shown that spirochaetes under the influence of various substances, or even spontaneously, are able to break up into granules. Noguchi observed such granule formation in pure cultures of the *S. pallida,* and also the development of spirochaetal forms from the granules after transference to a passive culture medium. Further, he claimed to have infected monkeys with syphilis from the spirochaetes resulting from the granules. These and other facts make it probable that the spirochaete may become granuloid during pregnancy. It is also possible that infection may occur through the granules instead of through the mature spirochaete, for Neisser observed that the tissues of syphilitic apes in which no spirochaetes could be found were capable of conveying infection. As Routh points out, any substance in the mother which is capable of exciting this spirillolytic action must be present very early in pregnancy to prevent immediate destruction of an ovum infected by the *S. pallida*, and it must also continue its action during pregnancy or there would be little chance of an infant being born alive. In 1914 Routh suggested that the chorionic ferments or their derivatives possess this granulosing power. The ferments assist the fertilized ovum to burrow into the uterine mucosa at the placental site, and Routh suggests that if they possess such a destructive action on the maternal tissues they might also act chemically on the spirochaetes and cause them to break up into granules. The granules, he believes, are kept biologically inactive by the ferments and do not develop into spirochaetes so long as the chorionic ferments are present. After pregnancy the ferments gradually disappear from both the maternal and foetal tissues, and the granules may resume their biological activity and develop into spirochaetes.

This theory will explain several anomalies of the Wassermann reaction. Thus: (1) the case of a woman who gives birth to a syphilitic child and has a negative Wassermann reaction during pregnancy and for some time afterwards, may be explained by infection by latent granules and not mature spirochaetes. Routh believes that such instances only occur when the ovum is infected by the father's semen—pure paternal infection. Some weeks after delivery, when the ferments disappear, spirochaetes may develop and form antibodies resulting in a positive reaction. The child of such a mother would also be negative at birth, and would remain so if the granules had been completely destroyed by the ferments; but if the latter were not destroyed spirochaetes might develop and produce a positive reaction shortly before the clinical symptoms of congenital syphilis. It is also possible that a previously syphilitic woman positive during pregnancy may have a child with a negative reaction, if the chorionic ferments or salvarsan, or both, have granulosed her spirochaetes and thus prevented them from invading the foetal tissues; (2) the occasional birth of an apparently healthy child in a series of dead or syphilitic children can be explained by the chorionic ferments causing absolute destruction of the granules; (3) a woman with a syphilitic husband who has infected the ovum at fertilization may become infected through the foetus, and may give a positive reaction if the ferments fail to protect her from spirochaetal infection; or, both she and the child may be protected during pregnancy by the ferments granulosing the spirochaetes, and both may remain negative till after the ferments have disappeared after parturition.

The occurrence of spermatic infection of the ovum, although not proved, is in Routh's opinion highly probable. That the semen may convey contagion has been shown by Finger and others, and more recently Pinard claims to have found the *S. pallida* in it. In any case, as Routh suggests, granules may be conveyed by the spermatozoa and kept latent by the chorionic ferments. In the case of mature spirochaetes conveyed by the semen these would be granulosed by the ferments, and both foetus and mother would only be infected by granules, and both would give negative reactions after parturition till the ferments ceased to act.

Treatment, in Routh's opinion, is only likely to be successful if, up to the date of its commencement, the multiplication of the mature spirochaete has been prevented by the granulosing action of the ferments, for the unimpeded action of the spirochaete on the early ovum or foetus would cause its destruction. Salvarsan, which has been shown by Balfour, O'Farrel, and others to cause granulosing of the spirochaetes, is, according to Routh, an adjunct to the action of the ferments. Treatment should be commenced as early in pregnancy as possible, but successful cases have been reported where it was not begun till the seventh or eighth month.

The value of the *Wassermann reaction in pregnancy* is discussed by Williams (2) on the basis of over four thousand consecutive cases observed between April 1916 and December 1919 at the Johns Hopkins Hospital. The percentage of positive reactions in this series was 11·2. The cases were divided into three groups; those who had no treatment, those who had insufficient treatment. and those who had efficient treatment. A course of five or six injections of salvarsan followed by mercury till the Wassermann reaction became negative was regarded as efficient. The infants resulting from these pregnancies were examined clinically and serologically by microscopic examination of the placenta and by autopsy. The good effect of treatment was shown by the fact that in the women who had received adequate treatment 93·6 per cent. of the infants were free from syphilis, while in those who had had no treatment 33·7 per cent. were definitely syphilitic, and 14·7 per cent. doubtful.

In 109 women in whom there was some evidence of syphilis, but a negative Wassermann reaction during pregnancy, there were four groups: (1) those who had a positive reaction in previous pregnancies and had been treated and apparently cured; (2) those where the autopsy of the infant showed syphilis; (3) those with evidence of syphilis in the placenta but an apparently normal child; (4) cases where the father gave a positive reaction. Of these 109 women 44 had been effectively treated in previous pregnancies and were regarded as cured of syphilis. The remaining 65 gave birth to 54 dead and 11 living infants. Of the 54 dead infants, 43 were autopsied and 40 showed evidence of syphilis. Of the 11 born alive 3 showed signs of syphilis. The remaining eleven were not autopsied, but some of them were probably syphilitic. Thus, of 65 infants born of mothers with a negative Wassermann reaction during pregnancy, 43 were definitely syphilitic. At first sight this would appear to invalidate the value of the reaction in obstetrics, but Williams remarks that all we can conclude is that about one child in 100 (43 out of 4,000) will have syphilis even when the mother has a negative reaction. The practical bearing of these results is stated by Williams as follows: If it be assumed that 11 per cent. of women have a positive Wassermann reaction, and that without treatment 50 per cent. of their children will be syphilitic, we should expect 55 syphilitic infants in every 1,000, and 10 others which would be born of women with a negative reaction, or a total of 65 per 1,000. Hence the figures indicate that even though a routine Wassermann test is made early on all pregnant women, and efficient treatment instituted at once, only five-sixths of the ideal results are obtained. This applies only to the first birth, as in the women with a negative reaction the existence of syphilis would be detected after the birth of the first child, and treatment instituted with good results. If we succeeded in reducing the foetal mortality from syphilis by five-sixths its eventual incidence would scarcely exceed one per cent.

With regard to the infants, the fate of 29 which gave a positive reaction at birth was followed up: 17 developed syphilis; 5 had no signs of syphilis but still a positive reaction; 7 had no signs of syphilis and the reaction became negative. The prognostic value of the foetal Wassermann reaction is also discounted by the after-history of those with a negative reaction at birth. Ten of such cases became positive. Hence we must conclude that a positive reaction at birth does not necessarily remain positive, and conversely a negative reaction at birth may become positive later. Therefore the information obtained by testing the foetal blood at birth is not worth while.

Microscopical examination of the placenta agreed with the clinical and anatomical findings in 80 to 90 per cent., as compared with the Wassermann reaction in the mothers, which only agreed in 40 per cent. Thus, examination of the placenta is twice as likely to give correct information as to the condition of the infant as a Wassermann test in the mother. Many children born of mothers with a positive reaction showed no signs of syphilis.

Dealing incidentally with the subject of spermatic infection, Williams mentions a remarkable case of twins which is highly suggestive. One of the twins showed definite signs of syphilis, the other was normal. The mother admitted having connexion both with her husband and with another man, and it is suggested that the twins might have been the product of different fathers: i. e. an instance of superfecundation. This view is supported by the fact that the woman had subsequently eleven healthy children with normal placentas and that the Wassermann reaction was negative in both husband and wife.

At a recent discussion on congenital syphilis at the Royal Society of Medicine, Morley Fletcher drew attention to the *change of type* in congenital syphilis. The number of infants with obvious manifestations, such as skin eruptions and condylomata, was much less than it used to be, although there was no diminution in the number of cases. Sir H. Rolleston suggested that this change of type was possibly due to some alteration in the strain of the spirochaete, which was attracted to the viscera and nervous system instead of to the skin.

**Symptomatology.** A case of *warty naevus* occurring in a heredo-syphilitic subject and improved by mercurial treatment is reported by Gougerot and Dessaux. The patient, a girl aged 12 years, presented linear warty naevi of the hand which had increased in extent since birth. The signs of heredo-syphilis were indefinite, but the Wassermann reaction was strongly positive. Under injections of calomel the more recent lesions disappeared, while the older and more warty lesions only yielded to cauterization. The authors mention that the frequency of heredo-syphilis in connexion with naevi was drawn attention to by Gaucher some time ago.

Stolkind has failed to find any definite evidence of *congenital syphilitic aortitis* in older children, adolescents or adults, although he admits that such cases may exist. He remarks that observers do not agree as to the pathological changes in congenital syphilis of the aorta, while the lesions of syphilitic aortitis in adults are characteristic. Also, he has found no reported case in which the *S. pallida* was found in the aorta of congenital syphilitics more than a year old. If congenital syphilitic aortitis really occurs in older children, he questions whether it is possible to diagnose it clinically. In a case he observed, a child aged 10 years with aortic stenosis, the mother gave a history of two abortions and there was a suspicion of congenital syphilis, but no signs of syphilitic aortitis were found at the autopsy. In another case, a girl aged 14 years with aortic regurgitation, there were definite signs of congenital syphilis—Hutchinson's teeth, syphilitic ulcers of the leg, and a positive Wassermann reaction. There was also a history of chorea. The autopsy showed pericarditis and endocarditis of the aortic and mitral valves probably due to chorea, but no signs of syphilitic disease of the circulatory system. Stolkind points out that a positive Wassermann reaction in cases of aortic regurgitation, or in cases suspected of aortitis or myocarditis, does not prove that the condition is syphilitic. In cases of syphilitic aortitis observed by him, in which an autopsy was made, some had suffered both from syphilis and articular rheumatism, and the post-mortem findings were either: (1) syphilitic aortitis alone or with aortic regurgitation; (2) lesions typical of the endocarditis of acute infections; (3) combined lesions of both groups. He concludes that the question of congenital syphilitic aortitis requires further research.

Hennebert reports three cases of *deafness due to congenital syphilis.* The onset of deafness was in early infancy in one case, at the age of 8 and 15 years in the other two cases; but, according to Hennebert, it may not appear till the second or third decade. All three cases showed definite signs of congenital syphilis—traces of old interstitial keratitis, syphilitic arthritis, &c. The degree of deafness varied, being only of slight degree in the first case, originating in infancy, much more marked in the second case, and total in the third case. According to Hennebert, in the majority of cases of deafness due to congenital syphilis, the pneumatic test is positive, the rotatory test negative, and the thermic test much diminished. In the third case, however, the thermic test was normal on both sides, showing that the vestibules were intact and the deafness might be due to a central lesion. He remarks that there is no way of distinguishing between deafness due to destruction of the cochlea and that due to deep lesions of the acoustic tracts.

Harman reports the associated symptoms found in 600 cases of *blindness due to congenital syphilis.* These cases comprised 398 of interstitial keratitis and 229 of disseminated choroiditis. In the group with interstitial keratitis the chief associated symptoms were: Hutchinson's teeth, 265; characteristic physiognomy, 115; iritis, 128; scars about the mouth, 61; bone or joint disease, 26; ulceration of nose or palate, 15; deafness, 63. In the group with choroiditis they were: Hutchinson's teeth, 97; characteristic physiognomy, 53; bone or joint disease, 19; deafness, 51. A family history of miscarriages, still-births, infant deaths, and diseased children was obtained in 170 of the keratitis cases, and in 115 of those with choroiditis.

Neame reports on the treatment of 24 cases of *interstitial keratitis* with arsenic and mercury. He found that in 5 cases the second eye became affected after this treatment, and doubts if treatment commenced before the second eye is affected will prevent it. He thinks, however, that it may prevent choroido-retinitis.

Parker reviews the literature of *juvenile tabes* and records seven cases of his own, which agree on the whole with those of other observers. In his seven cases the knee-jerk was absent in all; the Argyll Robertson pupil was present in three, loss of reflex both to light and accommodation in four, and optic atrophy in three; lightning pains and crises were present only in three cases; only one case showed ataxic symptoms; incontinence of urine was present in two. The Wassermann reaction was positive in the blood in all but one case. The cerebrospinal fluid was negative in three cases in spite of the presence of well-marked symptoms and a positive reaction in the blood ; in the other four cases it was positive. The ages of the patients varied from 7 to 19 years, and there were five males and two females. The first pronounced symptoms were vomiting in two cases ; blindness in three ; and pains in the joints in two cases. The author draws attention to the slow onset of the disease and its frequent termination in general paralysis. Juvenile tabes appears to differ from the tabes of acquired syphilis in the relative infrequency of ataxia, girdle pains, and lightning pains.

Mott found definite signs of congenital syphilis in half the cases of juvenile general paralysis and tabes which he examined, and obtained a history of syphilis in the majority. He often found a history of several miscarriages followed by the birth of a juvenile paralytic, who seemed to be the last development of the familial disease.

Cases of *transmission of syphilis to the third generation* in which the evidence is practically conclusive are rare, but the following case, reported by Paterson, appears to be a true example. A male child, aged 2½ years, had the characteristic facies of congenital syphilis, was mentally deficient, and had a positive Wassermann reaction. The mother also had definite signs of congenital syphilis—saddle nose, the remains of old keratitis, and external strabismus—and a positive Wassermann reaction. Her first child, now aged nine years, has no signs of syphilis, the second child is the one under consideration, then came a miscarriage, and lastly an infant, now aged two months. The father's Wassermann reaction is negative, and also that of the last baby. The maternal grandmother died of locomotor ataxia ; she had several children, the last two only surviving. It appears, therefore, that in this case the disease was transmitted from the grandmother to the mother, and then to the child. There was no evidence of reinfection of the mother.

**Diagnosis.** Lafaye, working in Marfan's Clinic, has compared the value of the *luetin reaction* with that of the Wassermann reaction in the diagnosis of heredo-syphilis. In cases with definite clinical symptoms he found the luetin reaction positive in only 30 per cent., while the Wassermann gave from 67 to 75 per cent. positive reactions. He remarks that the luetin reaction is difficult to interpret, and that the difference between doubtful and negative results is more theoretical than real ; that it is much less constant than von Pirquet's tuberculin reaction. He concludes that no value can be attached to a positive luetin reaction when the Wassermann reaction is negative and clinical signs are absent.

With regard to the bearing of the Wassermann reaction on treatment, he is of opinion that all cases of heredo-syphilis should receive systematic treatment, whether this reaction is positive or negative ; but that treatment should not be too intense or too prolonged merely on account of a persistently positive reaction.

As the result of systematic Wassermann examinations carried out at the Coast Hospital at Refsnaes in Denmark, Hertz has succeeded in weeding out as syphilitic a considerable proportion of cases sent to him as tuberculous. The reaction was positive in 2·25 per cent. of 1,610 cases, and among his cases of congenital syphilis masquerading as scrofulous or tuberculous were 13 of arthritis, 10 of fistulous adenitis, 10 of kerato-conjunctivitis, and 6 of rickets. A typical case was that of a girl, aged 12, who had been in one hospital for half a year, suffering from disease of the knee. At another hospital she developed disease of one elbow. Admitted to

Refsnaes, she was found to be suffering from congenital syphilis, and mobility of the joints was restored by specific treatment. After giving short notes of 8 other cases, Hertz points out that in every case the establishment of the right diagnosis led to specific treatment which was invariably successful. Most of his patients had flitted from one institution to another over a period of several years, and recovery was not effected till specific treatment was adopted. Among the cases of arthritis, the knee seemed to be most frequently involved, and among the diseases of the eyes, dacryocystitis was so frequently found associated with a positive Wassermann that Hertz learnt to suspect syphilis whenever he saw this condition. With regard to the aetiology of spina ventosa, he diagnosed syphilis only in two out of several hundred cases, and he compares this negative finding with the view advanced by Calot and Menard that syphilis is responsible for 50 per cent. of all these cases.

**Treatment.** The results of antenatal treatment of pregnant women at the London Lock Hospital, are reported by Rundle. Of 168 cases, 92 were infected with syphilis and 76 with gonorrhoea. The syphilitic cases were classified as follows: (1) late pregnancy with signs of general syphilis; (2) early pregnancy with signs of general syphilis; (3) early pregnancy with primary syphilis and a negative Wassermann reaction; (4) late pregnancy with primary syphilis and a negative reaction; (5) cases which had received a full course of treatment before admission; (6) cases with no signs of syphilis, but a history of miscarriages and a positive Wassermann reaction. The bad results were all in cases of the first class. In the 92 cases of syphilis there were 5 still-births and 9 infants which died soon after birth; the rest did well. The mothers were treated with intravenous injections of '914', and mercury was administered either by the mouth, by intramuscular injection of grey oil, or by intravenous injection of the cyanide. The last method consisted in 5 injections of 10 to 20 minims of a 1 per cent. solution every week for 8 weeks.

Indirect treatment of the infant by suckling while the mother received '914' proved more beneficial than direct treatment of the infant. As regards the latter, the external jugular vein was preferred to the veins of the scalp or the longitudinal sinus for intravenous injection of '914'. The infants were fed by the method of 5 daily feeds and an 8-hour rest at night.

Adams, reporting his results of three years' treatment of syphilitic mothers and infants, states that most of the infants were followed up and that many of them at the age of two years appear healthy and have a negative Wassermann reaction. Also, only one infant gave a doubtful positive reaction after once becoming negative. In each year the percentage of infants born with a negative reaction has increased, a fact which he attributes to more active treatment of the mothers. The results of treatment varied with the period in pregnancy at which it was commenced. In the last two years there was only one still-birth and no deaths from syphilis among the cases treated. Adams's experience is that if the mother's Wassermann reaction can be brought to negative or doubtful at her confinement the infant will be born negative and show no sign of syphilis, whereas, if the mother is positive the infant will probably be also positive. Exceptions, however, may occur, as in the following case: a woman with a definite history of syphilitic infection in the seventh month of pregnancy and no treatment during pregnancy gave birth to an infant with a negative reaction, although she had generalized syphilis with a positive reaction. None of the infants in Adams's series born negative have since become positive or developed any signs of syphilis, though many have had no treatment beyond the drugs absorbed through the mother's milk. Adams concludes that a pregnant woman with syphilis, whether active or latent, if treated for three or four months before confinement, will probably give birth to a healthy infant at full term.

The treatment adopted by Adams is as follows: (1) for the mothers, weekly intravenous injections of neosalvarsan or galyl, and mercury either in the form of weekly injections of 40 per cent. grey oil or grey powder by the mouth; (2) for the infants, 7 intramuscular injections of glucose-galyl, commencing with 1·5 cgm. and increasing to 3 cgm., the first two injections being given at a week's interval, the others at fortnightly intervals; concurrently with these, six intramuscular injections of grey oil in doses of $\frac{1}{4}$ to $\frac{1}{3}$ grain mercury at fortnightly intervals, and also $\frac{1}{2}$ grain of grey powder by the mouth daily. After an interval of six weeks, two supplementary injections of 5 cgm. galyl and $\frac{1}{2}$ grain of mercury are given. It was found that galyl mixed with glucose was well borne by infants. The Wassermann reaction was nearly always negative before the supplementary injections.

Intramuscular injections in the treatment of congenital syphilis are also advocated by Fordyce and Rosen, who consider that injections into the veins of the arm, scalp, or neck—or into the longitudinal sinus as recommended by some—may do more harm than good in the hands of the inexperienced. The methed they adopt consists in the intramuscular injection of neosalvarsan (neoarsphenamine) and an oily suspension of mercury, by means of a special needle with a shield, to ensure deposition of the drug in the gluteal muscles of the infant. The preparation of mercury used is the perchloride in doses of $\frac{1}{10}$ to $\frac{1}{8}$ of a grain, or larger for older children, mixed with palmitin in ampoules. The doses of neosalvarsan (neoarsphenamine) are 0·075 gm. for infants from 3 to 8 weeks old; 0·1 gm. for infants from 2 to 6 months old; 0·15 gm. from 6 to 12 months; 0·15 to 0·2 gm. from 1 to 2 years. The injections are given at weekly intervals. An average course consists of 6 injections of mercury and 7 of arsenic. In weakly children the mercurial injections are given first, in other cases alternately with the arsenical. The authors point out that a Wassermann test done ten days after birth is more reliable than one done at birth; also that a negative result does not contraindicate treatment in the presence of clinical symptoms.

Findlay remarks that although mercury alone will, in the majority of cases, cause a disappearance of the symptoms, and in a certain proportion of cases cause the Wassermann reaction to become negative, the combined treatment with mercury and salvarsan is far more efficacious. In a series of cases under three months of age treated with mercury alone he had a death-rate of 71 per cent. With regard to the modes of administration of mercury he considers inunction the best and far more effective than grey powder.

Of the different methods of treatment by salvarsan he prefers intravenous injection, owing to the pain caused by intramuscular injection. He makes no reference, however, to the intramuscular injection of glucose-galyl, which has been extensively used by Adams and others, and apparently causes very little pain. For intravenous injection he chooses the veins of the scalp in children under 18 months of age, using concentrated solutions, by which doses of 0·1 to 0·2 gm. can be given in 3 or 4 c.c. by means of a 5 or 10 c.c. Record syringe. Injection into the longitudinal sinus, which has some advocates, is, as Findlay remarks, a dangerous procedure, owing to the possibility of transfixion of the wall of the vessel and consequent cerebral irritation from escape of the drug and also the danger of septic meningitis. In children over two years of age, either the external jugular veins or the veins at the bend of the elbow may be chosen; but as it is difficult to immobilize the parts in younger children, an anaesthetic is usually required.

As regards dosage, Findlay considers the dose of 0·0005 gm. per kilo of body-weight, which was formerly recommended, too small. In infants he commences with 0·05 gm. of neokharsivan gradually increased to 0·15 gm. In older children, 0·2 or 0·3 gm. may be given. The injections are given weekly till the Wassermann reaction becomes negative. According to Findlay, this result depends on the duration of treatment rather than on the amount of the drug administered. In his cases, the percentage of negative reactions rose to 100 per cent. after a course of eleven injections. He has not had a case in an infant in which the reaction again became positive, even in cases re-examined up to three years afterwards. In older children, however, it is often difficult to obtain a negative reaction.

The mortality in infants treated with combined mercury and salvarsan was 37 per cent. as compared with the 71 per cent. in cases treated with mercury alone.

With regard to prophylactic or antenatal treatment, the results are also better with the combined treatment than with the older method by mercury alone. Treatment of the pregnant mother by salvarsan was first employed by Sauvage, who obtained 93 per cent. of healthy births. In ten cases treated by Findlay with mercury and salvarsan a healthy child was born in each case. The number of injections varied between 4 and 8. According to Findlay, mothers treated in this way continue to bear healthy children even when no treatment is given during further pregnancies.

Finally, as a measure to aid the general adoption of antenatal treatment and obtain the greatest number possible of healthy children, Findlay is a strong advocate of the notification of cases of still-birth and miscarriage.

Lafaye recommends *intravenous injections of neosalvarsan* in infantile syphilis, either into the external jugular vein, the veins of the scalp, or the dorsal veins of the foot. He points out, however, that these injections require care and patience and also competent assistance. He also points out that, owing to the rigidity of the external jugular and epicranial veins, puncture is liable to be followed by extravasation of blood. Hence, very fine needles are required. He gives several series of 5 to 10 weekly injections with intervals of about two months, the initial dose of neosalvarsan being less than 1 cgm. per kilogram body-weight, and the last dose from 1½ to 2 cgm. per kilo. The concentrated solution was used, in a syringe of 2 c.c. capacity. In 50 cases treated in this way there were 7 fatalities, one of which only was attributed to the effect of the drug, the others being due to syphilitic cachexia, acute hydrocephalus, septic abscess, broncho-pneumonia, and pulmonary tuberculosis. The reactions were not severe, except in one case where a 'nitritoid crisis' occurred, which yielded to adrenalin. Lafaye does not believe that arseno-benzene should be definitely substituted for mercury in the treatment of heredo-syphilis, but remarks that it has a more rapid spirochaeticidal action on the lesions, and that infants gain more quickly in weight after this treatment. In the case of infants under two months old, however, he recommends that arsenical should be preceded by mercurial treatment.

Dupérié reports promising results with the method of *subcutaneous injections of novarsenobenzol with novocain,* suggested by Poulard. This method consists in the injection of 15 cgm. of novarsenobenzol in solution in 1 c.c. of 1 per cent. novocain into the adipose tissue of the buttocks, daily or on alternate days. The cases treated by Dupérié included both heredo-syphilis and acquired syphilis in children aged from 8 to 14 years. It is interesting to note that these included two cases of chorea with positive Wassermann reactions, the choreic movements ceasing after 10 and 20 injections respectively.

Mengert reports favourably on the treatment of congenital syphilitic infants with *silversalvarsan.* The injections were made with a thin platinum-iridium needle and a Luer's syringe, in most cases into the temporal vein, sometimes into the frontal, cubital, external jugular, popliteal, or dorsalis pedis veins. Injections into the longitudinal sinus were considered dangerous. As the injections must be made rapidly, owing to the movements of the infant, concentrated solutions were employed. In a few cases intramuscular injections were given, but these appeared to cause severe and prolonged pain. In 98 per cent. of 250 injections it was found possible to inject intravenously. The local effects included infiltrations at the site of injection in a few instances, two of which were followed by necrosis, probably due to injury to the vein by the needle. Angioneurotic symptoms only occurred in one case, Herxheimer's reaction once, and 'spirochaete fever' once; otherwise there were no after-effects. The syphilitic symptoms present in the infants included eruptions, enlargement of the spleen, coryza, and rhagades of the mouth. The eruptions were the most rapidly influenced by the treatment, and the enlarged spleen least. The Wassermann reaction changed from positive to negative at the end of the first course of injections, and a negative reaction was obtained in cases which had been refractory to previous treatment with neosalvarsan and calomel. The dose of silversalvarsan was 0·006 gm. per kilogram of body-weight, 0·1 gm. was dissolved in 5 c.c. of sterilized distilled water and $\frac{3}{10}$ c.c. per kilogram given as injection. A single series comprised 10 injections at intervals of 5 days, the whole course of treatment consisting of three series, which was increased if the Wassermann reaction had not become negative. Mercury was not given, in order to test the action of the silversalvarsan alone.

Mengert has also tried 'sulphoxylatearsen' in doses of 0·07 c.c. per kilogram of body-weight administered intramuscularly in courses of 7 to 10 injections at intervals of 8 to 10 days. He considers this preparation, which is said to have a more prolonged action, useful for the continuation of treatment, and also in cases where intravenous injections cannot be given.

Jeans claims promising results from the following method of treatment, which he has carried out at the St. Louis Children's Hospital, U.S.A., for a period of four years. Mercury is given in the form of weekly intramuscular injections of the perchloride (0·03 c.c. of a 1 per cent. solution for each kilogram of body-weight); also as grey powder in doses ranging from $\frac{1}{5}$ grain for small infants up to 2 grains for larger children, three times a day. Every two months three weekly intravenous injections of arsphenamine are given in doses of 0·01 gm. for each kilogram of body-weight. Mercury is continued during these courses. A rest of four to eight weeks is given in the first year of treatment. Infants continue the treatment for at least a year, and older children for at least two years, regardless of the Wassermann reaction; but it is considered desirable to continue for six months after all signs of activity, including the Wassermann reaction, have disappeared.

The cerebrospinal fluid is examined before arsphenamine is administered, and if it shows evidence of involvement of the central nervous system, arsphenamine is preceded by several weeks of mercurial treatment. This systematic examination of the cerebrospinal fluid revealed the fact that the central nervous system is involved in about one-third of the cases. In cases of hereditary neurosyphilis which do not improve after several months of the above treatment intraspinal treatment is given as well. Jeans considers that the arguments which have been adduced against the efficacy and rationale of intraspinal medication are founded on inadequate and conflicting evidence, and it is his impression that this treatment is beneficial. The method he now adopts comprises alternate weekly injections of salvarsanized serum (Swift-Ellis method) and Byrne's mercurialized serum. The course consists of three injections, and is repeated every two or three months. The general treatment is not interrupted during these courses.

Jeans emphasizes the importance of care in the nutrition of syphilitic infants, and points out that, although the nutrition generally improves with antisyphilitic treatment, intensive treatment occasionally has a harmful effect. In such cases the treatment should be modified or suspended. In cases of florid syphilis in infants he warns against using full doses of arsphenamine, which should be given at first only in small doses. In administering arsphenamine he prefers intravenous injection into the scalp veins or external jugular in infants, and the arm veins in older children. Injection into the longitudinal sinus he condemns.

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## STATISTICS RELATING TO THE TREATMENT OF CANCER OF THE BREAST BY EXCISION SUPPLEMENTED BY RADIATION

Statistical evidence shows that the treatment of cancer of the breast, based on the assumption that it is a disease of local origin, reached a stage of success some years ago beyond which it is difficult to demonstrate that an advance has been made.

Excision fails to cure in more than half the cases; the patient's death is directly due to the original disease. Failure is attributable to the excision being done too late; but in many cases delay has been due to the disease not having been previously noticeable, in respect of which there is no chance of improvement. As for the cases in which there has been delay after something abnormal has been noticed in the breast, if there were a greater number of patients cured, fewer would delay submitting to excision. Distinctions are made by clinical examination, as well as by microscopic examination after removal, but when applied to individuals these distinctions prove untrustworthy.

It would seem at the present time that opinion can only be based upon statistical enumerations in which individual variations are reduced to an average. This consideration applies to the question of the treatment by radiation supplementary to excision. At the present moment there is positive evidence that in individuals recurrences of cancer in the scar and neighbouring glands have disappeared under applications of X-rays and of radium, and the patients have remained free from further return of the disease. But in other individuals radiation has entirely failed, and assertions have been made that malignant growth has been stimulated and metastases widely distributed because the radiation has weakened local resistance and diminished general nutrition.

Success in the arrest by radiation of superficial disease has suggested the use of more penetrating rays to arrest disease, not only in the scar and axilla, but in the supraclavicular fossa and anterior mediastinum, as well as to prevent distant metastasis. As there is then nothing visible or palpable which is made to disappear, no conclusions can be based on individual observations at all.

To establish treatment by radiation as a supplement to excision, there must be support from statistical evidence; instances of individual successes or failures, arguments from analogy and hypotheses, do not satisfy.

In this country statistical evidence as regards radiation is singularly wanting. Sampson Handley, for instance, writing in 1919, said: 'During the last fourteen years every case of breast cancer upon which I have operated has received a prophylactic course of X-rays.' He presumed that the X-rays were calculated to arrest the permeation of the disease through lymphatic spaces in areas immediately outside that of the excision. More recently deeper radiation has been advocated, also the insertion of radium in the axilla, supraclavicular fossa, and anterior mediastinum. Yet up to the present there has been no statistical publication of results obtained in this country extending over years.

Bearing on the question of combining X-ray and radium in the supplementary treatment by radiation, the reports for the last 4 years by Pinch at the Radium Institute (*vide* table) suggest that, using radium alone, it is difficult to advance beyond a certain stage of success.

| | 1916. | 1917. | 1918. | 1919. |
|---|---|---|---|---|
| Cases examined but not treated | 8 | 6 | 5 | 7 |
| ,, without recent reports | 17 | 2 | 12 | 12 |
| ,, of prophylactic radiation | 12 | 4 | 7 | 5 |
| ,, apparently cured | 6 | 1 | 3 | 2 |
| ,, improved | 67 | 39 | 52 | 50 |
| ,, not improved | 24 | 7 | 13 | 13 |
| ,, who abandoned treatment. | 24 | 2 | 4 | 2 |
| ,, dead | 14 | 8 | 9 | 4 |

Passing to America, Deaver's work includes statistics from many sources relating to the results of excision before the supplementary use of radiation. The best appears to be furnished by Halsted's table.

204 operations, 13 lost sight of, 191 reported on, 39 (20 per cent.) alive

and well over 5 years from the excision. 10 died within the 5 years without recurrence of the cancer, but 10 suffered from metastases and died over 5 years after the excision.

In favour of supplementary prophylactic radiation Deaver noted individual cases in whom radiation had checked or completely removed local recurrences. He also mentioned 16 private case treated by Dachtler in which the operating surgeons had certified that at the time of excision the axillary glands were not diseased. Moreover, application of X-rays had been continued as long as was deemed sufficient. Of the 16, 13 were alive and well after 5 years, 3 had died meanwhile, but were found by post-mortem examination to be free from cancer. As to the results in such selected cases in which evidence of disease cannot be found in the axillary glands, when treated by excision only, there are statistics recording survival for over five years in as many as 85 per cent. of the cases.

Quick related the results of combining radiation by X-rays and by radium in 57 cases after excision for local recurrence or metastasis, also in 20 inoperable cases, and in one case which declined excision.

The 57 cases of recurrence and metastasis included local flat recurrences treated by X-rays and radium emanations, bulky recurrences in the axilla for which radium was embedded and also deeply penetrating rays used.

5 cases remained clinically free after the disappearance of a local recurrence, for periods varying between 3 months and 2 years.

13 cases improved but were not freed from the recurrence; all had been treated for 5 months.

19 cases received temporary benefit for periods of from 2 months to 2 years, then aggravation of the local disease and distant metastases supervened.

9 exhibited no improvement.

4 had been under treatment for less than 4 months.

7 had been lost sight of.

The 20 cases deemed inoperable were treated by combining X-rays with the embedding of radium.

1 was clinically free after 6 months; the diagnosis had not been confirmed by the microscope.

8 exhibited clinical improvement.

5 exhibited temporary clinical improvement.

1 failed to improve.

3 had been under treatment for less than 4 months.

2 had been lost sight of.

The one case who refused excision, in whom there was a mass without enlargement of axillary glands, and in whom the diagnosis was not confirmed by a microscopic examination, had the mass reduced to a dense cicatricial tissue, whilst she continued in good health.

The largest amount of statistical evidence relating to radiation supplementary to the excision of mammary cancer has been published in Germany. Blumenthal gave the results of post-operative radiation at the Charité in Berlin within the years 1915–1919. All the cases had undergone a radical excision by various surgeons, the majority at the Charité, the minority by outside practitioners.

1915. 60 cases.

12 had already been X-rayed elsewhere, of whom 7 already had metastasis, 3 developed metastases under treatment, and 2 continued free from disease.

6 were sent direct for radiation, of whom 2 had already metastases, 2 developed recurrence and metastasis under treatment, and 2 continued free from disease.

42 had already recurrence.

Result to the end of 1919: 15 (25 per cent.) continued free from recurrence and metastases.

1916. 63 cases.

9 already X-rayed elsewhere, of whom 3 had already recurrence, 5 had already metastases, and 1 continued free.

8 were sent direct for radiation, of whom 2 had already metastases, 3 developed recurrence and metastases, and 3 continued well.

46 had already recurrence.

Result to the end of 1919: 23 (36·5 per cent.) continued free from recurrence and metastases.

1917. 64 cases.

11 had been X-rayed elsewhere, of whom 4 had already recurrence, 6 had already metastases, and 1 continued free.

11 were sent direct for radiation, of whom 7 had already metastases, 1 developed metastases, and 3 continued free.

42 had already recurrence.

Result to the end of 1919: 29 (45·3 per cent.) continued free from recurrence and metastasis.

1918. 77 cases.

25 had been already X-rayed elsewhere, of whom 4 had already recurrence, 10 already metastases, 6 developed recurrence and metastases, and 4 continued free.

31 were sent direct for radiation, of whom 4 had already metastases, 6 developed recurrence and metastases, and 21 continued free.

Result to the end of 1919: 31 (40 per cent.) continued free from recurrence and metastases.

1919. 60 cases.

Result to the end of the year: 46 (76·6 per cent.) continued free from recurrence and metastases.

Allowing for the shorter periods after operation, Blumenthal's later results do not show an advance in the success of radiation over that obtained in 1915, and on the whole are not appreciably better than some attained by excision alone.

Tichy reported cases at Marburg under the following headings. Group I from the year 1904 to 1914, which were not X-rayed after operation. Group II from 1914 to 1917, the scar X-rayed at least once, or the scar, also the axillary and supraclavicular region, X-rayed several times. Group III in 1918 and 1919 intensively X-rayed after operation.

| | I. | II. | III. |
|---|---|---|---|
| Total number . . . . . . . | 62 | 36 and 25 | 11 |
| Recurrence within 1 year . . . | 7 (11·2 %) | 23 (37·7 %) | 5 (45·5 %) |
| Metastases developed . . . . | 3 (4·8 %) | 7 (12·1 %) | 2 (18 %) |
| Recurrence within 3 years . . . | 20 (32·2 %) | 37 (60·6 %) | |
| Late recurrence . . . . . | 1 after 9 years | | |
| Free from recurrence after 3 years . . | 24 (38·7 %) | 23 (37·7 %) | |
| ,, ,, ,, 5 years . . | 13 (20·9 %) | 19 (31·8 %) | |

On the face of it these statistics show an increase of early recurrence and of metastases since the introduction of radiation. Against this it may be claimed that owing to the war the women were operated upon at a later stage and were less well nourished.

Statistics furnished by Perthes and by Neher concerning cases at Tübingen were arranged in the same way as the preceding ones. Group I included cases submitted to radical excision in the years 1910–12 which were not X-rayed; Group II during 1913–16 lightly X-rayed, Group III from 1916–18 intensively X-rayed.

| | I. | II. | III. |
|---|---|---|---|
| Total number . . . . . . . | 130 | 144 | 72 |
| Recurrence within 1 year . . . . | 37 (28 %) | 55 (38·2 %) | 30 (41 %) |
| ,, ,, 3 years . . . . | 62 (47·5 %) | 78 (54·2 %) | |
| Metastases without local recurrence . | 14 (11 %) | 18 (12·6 %) | 13 (18 %) multiplicity of internal metastasis very marked |
| Free from recurrence after 3 years . . | 50 (38·5 %) | 44 (30·5 %) | |
| ,, ,, ,, 5 years . . | 36 (27·7 %) | 5 (20·3 %) | |
| ,, ,, ,, 6 years . . | 32 (24·6 %) | No case of recurrence after 6 years. | |

In 27 cases the primary tumour was not larger than an egg, it was adherent neither to the skin nor the pectoral muscle, and there was no clinical evidence of enlarged glands. Of these 27, 23 (85·2 per cent.) were alive without recurrence or metastasis over 3 years after the operation, 1 died of the operation, 2 died without recurrence, and 1 (3·7 per cent.) died of recurrence.

Of the cases in which supraclavicular glands were removed, whether X-rayed or not, only one remained alive and free from recurrence; all the rest were dead.

Kästner grouped the cases under Payr at Leipzig in the same way. Recurrence within the first year after the operation was not diminished, so that Payr had for the time being dispensed with a costly procedure.

| | I. | II. | III. |
|---|---|---|---|
| Total cases . . . . . . . | 69 | 22 | 42 |
| Recurrence within 1 year . . . . | 33 % | 36 % | 47·6 % |

A different arrangement was adopted by Lehmann and Scheven in publishing the experience over cases at Rostock, and by Hoffmann on cases at Heidelberg. The classification was made in accordance with the clinical examination previous to the operation.

Lehmann and Scheven's classification:

I. Mobile tumours without clinical evidence of enlarged glands.
II. Tumours adherent to skin or muscle or with enlarged glands.
III. Tumours adherent to skin and, or, muscle, and with enlarged glands.
IV. Tumours with enlarged supraclavicular glands.

| | | | | | |
|---|---|---|---|---|---|
| I. | Free from recurrence after 3 years. | Not rayed | 61·5 % | X-rayed | 80 % |
| II. | ,, ,, ,, | ,, | 27·1 % | ,, | 45·7 % |
| III. | ,, ,, ,, | ,, | 7·6 % | ,, | 27·7 % |
| IV. | ,, ,, ,, | ,, | 0 | ,, | 0 |
| | Average . . . . . . . | ,, | 32·7 % | ,, | 47·5 % |
| | Free from recurrence over 5 years . . . | | 27·7 % | | |

Hoffmann's report on cases at Heidelberg was a continuation of those extending over 40 years.

Since 1915 prophylactic radiation had been carried out in all cases, as well as X-ray and radium treatment for recurrence.

Group I included tumours not larger than a walnut, of slow growth, not adherent to deep structures, not adherent or only slightly adherent to the skin, and without evidence of enlarged axillary glands.

Forty cases within the previous 20 years. 12 (30 per cent.) died within 3 years, 24 (60 per cent.) were alive and free from recurrence after 5 years. The cases which died of recurrence were chiefly those first diagnosed as cases of fibroadenoma. The subsequent radiation appeared to afford no better results than had been previously achieved by excision alone.

Group II included cases more or less extensively adherent to the skin and pectoral fascia, with axillary glands perceptibly enlarged.

58 cases were not prophylactically X-rayed after operation; of these, 29·3 per cent. were alive and free from recurrence over 3 years.

49 cases were prophylactically X-rayed and 40 per cent. were alive and free from recurrence over 3 years after.

Under this group, therefore, there was a 10 per cent. improvement in those prophylactically X-rayed.

Group III were cases in which the cancer involved the whole breast, extensively adhered to the skin and pectoral muscle, and had already invaded the axillary and in some cases also the supraclavicular glands.

66 cases of whom 60 died within 3 years, 3 between 3 and 5 years, and 3 were alive without recurrence over 5 years. One of these last was a bilateral case, and in two the supraclavicular glands were removed.

The prophylactic X-raying produced no improvement over treatment by excision alone, but there was no evidence of harm done by the radiation.

Brattström reported the cases which had been operated upon at Lund between 1898 and 1915. Supplementary radiation treatment had only been systematically adopted after that period.

| | 1898–1905. | 1905–1915. |
|---|---|---|
| Total cases | 84 | 212 |
| Died after operation | 1 | 1 |
| Unheard of | 6 | 13 |
| Recurred and died | 50 | 133 |
| Free from recurrence over 3 years | 27 | 63 |
| Later recurrence | 2 | 5 |

Combining the series and so far as known.

| | |
|---|---|
| Survival free from recurrence over 3 years | 29·3 % |
| ,, ,, ,, 5 years | 23 % |

Boss divided the Breslau cases in the same way as Hoffmann's Heidelberg cases.

| | | |
|---|---|---|
| Group I | 23 cases | 70 % survived 3 years |
| ,, II | 69 ,, | 60 % ,, ,, |
| ,, III | 15 ,, | 14 % ,, ,, |

At Breslau the general conclusions as to radiation were that scirrhous and allied cancers, when they recurred locally, were amenable to X-ray treatment and the disease might be arrested. Infiltrating and medullary cancers tending to internal metastasis were refractory to radiation.

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# THE POST-MORTEM EXAMINATION OF A CASE OF ARTERIO-VENOUS ANEURYSM BETWEEN THE INTERNAL CAROTID ARTERY AND THE CAVERNOUS SINUS

**Arterio-venous aneurysm at the termination of the internal carotid.** The aneurysm is referred to under the following names: cavernous, orbital, ophthalmic, or intracranial aneurysm, also as pulsating exophthalmos. Post-mortem examinations of the condition have been remarkably few. Since Rivington's collection of cases in 1875, in which thrombosis of the cavernous sinus and of the ophthalmic veins, also the other causes of pulsating exophthalmos, were not clearly distinguished from aneurysm, there have appeared in English literature only clinical records. Therefore the post-mortem examination of a case by Seyfarth, accompanied by a good photograph and schematic drawing of the aneurysm is important. For the late war has been the occasion of accidents which have produced a pulsating exophthalmos. A brief notice of previously recorded post-mortem examinations may be recalled, although lacking in detail. In 1855, Nelaton's first case died some months after the *left* lower eyelid had been penetrated by the ferrule of an umbrella, upon which a pulsating exophthalmos developed on the *right*, the opposite, side. The man had recurrent attacks of nose-bleeding until he died. The sphenoid bone had been perforated and a splinter of bone had been driven into the cavernous sinus, where it had punctured the internal carotid artery. The cavernous sinus communicated with the sphenoidal sinus and so with the nose. The cavernous sinus was dilated, also the ophthalmic vein and its tributaries, which were tortuous.

Nelaton's second case was caused by a fall from a wagon; there was a hole 2 mm. in diameter in the internal carotid artery, within the cavernous sinus.

In Hirschfeld's case death occurred from erysipelas two months after a fall from a carriage upon pavement. The cavernous sinus was filled with clot and there was a small round hole in the carotid, as if it had been punched out.

In Leber-Schlaefker's case the aneurysm had been caused by a small shot. The internal carotid within the cavernous sinus was dilated to the size of a bean, and communicated at its outer and anterior side with the cavernous sinus by a hole freely admitting a No. 3 catheter.

Stuelp, in 1895, a pulsating exophthalmos having followed fracture of the base of the skull, found an opening with smooth edges, almost of the diameter of a pea, between the internal carotid and the cavernous sinus.

In Guibert's case the prong of a hay-fork had driven a splinter of bone into the carotid. Death occurred after three months, when an arterio-venous aneurysm was found between the internal carotid and the cavernous sinus.

Grut and Tscherning, in 1896, found a communication between the internal carotid and the cavernous sinus, the size of a hemp-seed, caused by a fall from a wagon. There was dilatation of the cavernous sinus and of the communicating ophthalmic vein.

In Nuel's case, in 1901, the penetration of the ferrule of an umbrella set up paralysis of the 3rd nerve and cerebral disturbance; death supervened three months later with apoplectic symptoms. An arterio-venous aneurysm between the internal carotid and the cavernous sinus had burst.

In 1904 Usher examined a case of pulsating exophthalmos which had followed a blow on the head, and in which death had occurred two days after the ligature of the external and internal carotids. There was a wide communication between the carotid and the sinus.

In Jack and Verhoff's case death followed four weeks after the ligature of the common carotid. There was an opening 3·25 mm. in diameter in the internal carotid, connecting an arterio-venous aneurysm with the cavernous sinus.

**Seyfarth's case.** A miner, aged 22, had had his head forcibly squeezed anteroposteriorly, which had caused a fracture of the base, after which he was unconscious for three days, and in hospital for six weeks. The right eyeball became pushed downward and forward and he complained of a continuous whirring noise; there was neither pain, nor epileptiform attacks, nor other disturbance. Four years later he wanted to marry, and he applied to the Eye Klinik in Leipsig to be relieved of the proptosis. The right eyeball was pushed downward and forward; there was marked chemosis of both eyelids; under the upper margin of the orbit were dilated and tortuous veins which pulsated, and there was a similar pulsating mass above the orbit in the middle of the forehead. There was a thrill and the most marked pulsation immediately below the right upper margin of the orbit, which was arrested by compression of the carotid on that side. The right internal and external carotid were first tied, and then the varicosities on the forehead were transfixed by deep sutures. As pulsation continued, 10 days later the varicosities on the forehead were transfixed with 10 magnesium needles. Upon this severe septic inflammation set in, followed by pyaemia and death after nine days. There were multiple abscesses in the lungs, but the venous sinuses and jugular veins were not affected, so that the aneurysm had not undergone any change *sub mortem.* A photograph of the aneurysm under the dura mater was made after removal of the brain. Then the dura mater was removed, the carotids and jugulars irrigated from the neck, and the aneurysm dissected. The schematic drawing explains the description given. In the middle cerebral fossa, to the right of the sella turcica, there was an aneurysm which had raised the dura mater and corresponded to the size of a walnut. Behind the posterior clinoid process the aneurysm had bulged towards the middle one, so as to rest on the clivus of the sphenoid, forming a diverticulum the size of a hazel-nut. After the removal of the roof of the orbit, also fat and muscle. the ophthalmic vein and its tributaries appeared as a tortuous mass, veins being dilated up to a diameter of 12 mm., so as to nearly fill the orbit, and these communicated with tortuous veins in the eyelid and on the forehead. The main aneurysmal tumour, the size of a walnut, was divided into two halves by a septum. The anterior half had been formed by a dilatation of the internal carotid to the size of a hazel-nut just after its entry into the sinus out of the bony canal. Up to this point the artery was occluded by a firm clot which had extended from the ligature upward. Beyond the dilatation where the artery passed through the dura mater it was of normal size. This dilatation had a smooth lining and there was no sign of clot; in front it communicated with the dilated ophthalmic vein by a round opening the size of a linseed. Behind it communicated through the septum with the posterior half of the aneurysm by a hole which admitted a medium-sized catheter. The posterior half of the aneurysm was formed by a dilatation of the right cavernous sinus, forming a loculated cavity, with a smooth lining, quite free from clot. The largest loculus bulged back upon the clivus and communicated with the circular sinus. The right ophthalmic vein opened into the dilatation of the cavernous sinus, the orifice being 10 mm. in diameter. The communication of the vein with the carotid, mentioned above, was situated just before its termination. There were no remaining signs of a fracture of the base, only some thickened strands fixing the dura mater to the skull in the middle cerebral fossa.

The description by Seyfarth is by far the best hitherto recorded, and so far tends to explain some of the conditions observed clinically, especially the extension towards the opposite side, owing to communication through the circular sinus and into the tributaries of the opposite ophthalmic veins, also to the veins on the forehead.

Cauchoix recorded a case of pulsating exophthalmos which was cured by the ligature of both common carotids, with an interval of three months between the two operations. He then added a collection of 16 cases of bilateral ligature, the intervals varying between 5 and 16 months. Only in one case was the bilateral operation done at the same time; the patient died two days later after exhibiting signs of paralysis and blindness. Among the cases were two deaths from hemiplegia following the second ligation, and four of survivals with impairment of vision, loss of an eye, hemiparesis, aphasia; six made a progressive improvement, and two were cured. In three the bilateral ligature failed to alter the pulsating exophthalmos. There are of course many more on record than those noted by Cauchoix, but mostly the publication has been very soon after the operations. Cauchoix added that in nine cases in which a bilateral ligature had failed, attempts to relieve the venous dilatation are said to have induced improvement. Seyfarth's case illustrates the danger involved in such a procedure.

**Cauchoix, A.** Exophthalmos pulsatile traumatique; ligature des deux carotides primitives; guérison. *Bull. et mém. Soc. de chir. de Par.*, 1921, **47**, 153, 222.

**Seyfarth, C.** Arteriovenöse Aneurysmen der Carotis interna mit dem Sinus cavernosus. *München. med. Wchnschr.*, 1920, **67**, 1092.

W. G. S.

## THE RÔLE OF ANOXAEMIA IN THE PRODUCTION OF SYMPTOMS IN DISEASE AND INJURY OF THE NERVOUS SYSTEM

Speaking of the effects upon the organism of want of oxygen, Bayliss remarks in his reference to the well-known observations of the Pike's Peak Expedition that 'The psychical disturbances are often like those of alcoholic intoxication; unreasonable behaviour on the part of visitors required the presence of a deputy-sheriff on Pike's Peak', and he adds, 'Perhaps unreasonable people met with under ordinary circumstances are really suffering from want of oxygen.' There is probably more truth in the epigram than the neurologist, with his somewhat rigid conceptions of the mechanism of symptom production in disorders of the nervous system, would be prepared to admit.

However this may be, for many years now observations have been accumulating on the psychical and neurological symptomatology of reduced atmospheric pressure, of CO poisoning, and of diminished oxygen tension in inspired air; in a word, of conditions in which oxygen want or anoxaemia is the essential factor. It is true that in none of the observations have neurological or psychological problems been directly under investigation. In most instances, indeed, disordered action of the nervous system has presented itself as a complicating factor encountered by observers when subjecting themselves to the atmospheric conditions in question. This may be seen in observations as diverse as those of Tissandier, the balloonist, and the more recent observations of Haldane and his co-workers. During the war, the subject received more direct attention from medical observers when the effects of flying at high altitudes provided a problem of serious importance, and the observations of Birley and others in France at this time should prove full of significance for neurologists.

Nevertheless, neurological literature may be searched in vain for any adequate discussion of the part which oxygen want may conceivably play in the genesis of disorders of nervous function. A notable exception is provided by an article on the pathological physiology of the skull and brain by Trotter in Choyce's *System of Surgery*. Trotter refers to the important part played by cerebral venous congestion in the production of so-called irritative cerebral symptoms. These, he emphasizes, are not due to excessive stimulation of cortical or other centres, but to hyperexcitability or exaggerated response to ordinary stimuli. Thus the Jacksonian fits sometimes seen after a depressed fracture over the Rolandic cortex are not due to direct irritation of this by indriven spicules of bone, as is so commonly assumed, but to interference with adequate oxygenation of the compressed cortex. Experimental physiology lends no support to the view that mechanical stimulation of the motor cortex can excite response. The convulsions of asphyxia are a striking confirmation of this point of view. Undoubtedly, also, the convulsions associated with a developing cortical thrombosis, or with grave haemorrhage remote from the skull, owe their origin to the same cause, namely, a mild grade of oxygen want, leading to increased excitability of the region of brain affected.

In admitting that we know very little, as neurologists, of anoxaemia as a factor in symptom production in disease or injury of the nervous system, we must allow that we have by no means exhausted simple physiological factors in the explanation of both psychological and somatic neurological disturbances of function. This admission, once made, would be full of significance for neurological research at a moment when fashion dictates that we shall invoke psychogenesis or phylogenesis for the elucidation of all symptoms, including those as far removed in character as infantile constipation and Jacksonian fits.

Pawlow's important experiments on the formation of 'conditional' reflexes show how fruitful the application of the methods of physiology may be in exploring territories hitherto appropriated by the psychologist, and utilized by him for little else than the cultivation of a rank growth of verbiage. Pawlow's views on this important matter are well worth quotation. He says, 'During our many years of work we have never been able with advantage to turn to psychological conceptions for help, or to utilize explanations founded on these conceptions. . . . Such help as psychology gives consists only in words; the animal has remembered, he has desired, he has thought—in other words, these were merely examples of undetermined thought'. And again, 'For an exact and continuous scientific investigation of the functions of the higher nerve centres, it is necessary that the fundamental and guiding principles be purely physiological ones.' Similar objections might be urged against the widespread appeal to phylogenetic factors, especially when these involve hypotheses which find no confirmation in the observed facts of comparative physiology and anatomy.

**The effects of anoxaemia on the spinal reflex mechanism.** A considerable amount of exact work has been done upon the effects of asphyxia on the reactions of the cord in the spinal animal. In such a preparation we may study the effects of anoxaemia in their simplest and most uncomplicated form. Perhaps the earliest work was that of Brown-Sequard, who, in his researches into epilepsy, produced 'epileptic fits' in guinea-pigs by various peripheral and central nervous lesions. He also found that asphyxia produced these 'fits'. Recent investigations by Graham Brown have shown that these so-called 'fits' are really rhythmically repeated scratch reflexes, and this observer found that the mild degree of asphyxia associated with ether anaesthesia often induced a spontaneous scratch reflex. Sherrington also found that. in the decapitated cat, asphyxia facilitated the appearance of the scratch reflex, which often broke out apparently spontaneously. He concludes that, 'we may infer that in the decapitate preparation the condition responsible for the hyper-excitability of the reflex is lack of oxygen'.

In their observations on the effects of asphyxia on the spinal animal, Kaya and Starling attempted to dissociate the action of the two factors present in asphyxia; namely, excess of $CO_2$ and poverty of oxygen in the blood. They found that in the presence of abundance of oxygen excess of $CO_2$ did not increase spinal reflex activity, but tended finally to reduce it and to induce narcosis. But oxygen want, when the $O_2$ tension fell below 5 per cent., induced convulsions. They concluded that the medullary centres, and possibly also the higher centres, have evolved a specific sensitiveness to $CO_2$ increase, but that the spinal centres, while sharing with the rest of the nervous system 'the primitive function of excitation by lack of oxygen', are not specially sensitive to $CO_2$ increase. So that in asphyxia all the medullary centres are excited by the $CO_2$ increase to a general but co-ordinated discharge; and the accompanying oxygen starvation excites some lower spinal centres, producing general muscular spasm, which breaks into and confuses the co-ordinated respiratory rhythm arising in the medulla.

Mathison has amplified these observations by investigating the effects on the spinal reflex mechanism of oxygen want, of $CO_2$ inhalation, and of the injection of such weak acids as lactic acid into the circulation. The preparation he used was the decapitated cat. In such a cat, in which reflexes were not readily elicitable, he found that the administration of nitrogen—that is, deprivation of oxygen—produced marked facilitation of reflex activity, so that spontaneous scratching and flexion-extension movements of the limbs appeared. After thirty seconds of nitrogen forceful rhythmic movements of the hind limbs appeared, and on several occasions spontaneous evacuation of urine was associated with these movements. This phase of co-ordinated phasic reflex activity preceded the appearance of general tonic spasm of the limbs with opisthotonos or emposthotonos. The injection of weak acids gave similar results. On the other hand, excess of $CO_2$ in the inspired air, with adequate oxygen supply, did not facilitate reflex activity. He concludes, therefore, that oxygen want is the main factor responsible for the production of hyper-excitability of the spinal mechanisms, and that this condition is probably associated with the formation of acid products in the nervous centres. Hence the effect produced by acid injections. Lovatt Evans, making use of the fact that sublethal doses of the cyanides owe their toxic effects to the production of anoxaemia, has confirmed Mathison's observations as far as the spinal reflex mechanisms are concerned.

All these observations indicate that the isolated spinal cord, already cut off from higher control, is rendered hyper-excitable by anoxaemia. Analysis of this activity shows that it includes the appearance of spontaneous co-ordinated reflex movements and also of what has been called visceral facilitation (evidenced by the passage of urine), though Barrington's observations warn us against regarding such a passage of urine as a true act of micturition, since the spinal animal is incapable of it. Clearly, the investigation of these phenomena from the point of view of motor reactions of the skeletal musculature is incomplete and calls for further investigation, but even with the limited knowledge at our disposal we cannot but be struck with the resemblance between the facilitation of reflex activity by anoxaemia and the 'mass reflex' seen in spinal man after the isolated cord has emerged from spinal shock. This, it will be recalled, has been regarded as representing the reappearance in its primitive form of a phylogenetically old mode of motor response: of a primitive defensive movement-complex. Various objections to such a hypothesis have already been considered in a review on the physiology of the elementary nervous system (*Medical Science*, 1921, **4**, 141), and will not be further discussed here. However, it seems reasonable to point out that, before we fall back upon speculative phylogenetic explanations, the simple physiological factor under discussion must be eliminated as an agent in the causation of the remarkable reflex hyper-excitability of the isolated cord in man. Is it too far-fetched to suppose that division of the cord and rupture of the theca by the brutal method of the gunshot wound may have some effect upon the vascular supply of the isolated segments of the cord?

This would not need to be severe, for it is only the milder grades of anoxaemia which produce hyper-excitability, severer grades depress function. The marked chromatolytic changes in the motor nerve-cells of the isolated cord are well recognized, and it has been the custom to attribute them to spinal shock, or 'isolation dystropy'. Nutritive disturbances resulting from vascular defect would provide an equally reasonable and not more speculative explanation. Until these problems have been directly investigated no final judgement can be passed upon them.

**Anoxaemia and cerebral activity.** Barcroft, in an admirable summary of the effects of anoxaemia upon the organism, more particularly upon the brain, quotes Haldane as saying that 'anoxaemia not only stops the machine but wrecks the machinery', the machine in this instance being the brain. Barcroft concludes that acute, almost complete anoxaemia of short duration does not cause permanent damage unless it be severe enough to produce prolonged unconsciousness. He quotes a case of the superior longitudinal sinus syndrome of Holmes and Sargent, in which the motor areas on both sides were asphyxiated for 36 hours, but in which but slight residual defect of function remained. He compares the effects of acute mild anoxaemia to those of alcoholic intoxication; acting either by inhibiting the higher centres or by poisoning these so that lower centres gain control. Chronic anoxaemia on the other hand simulates fatigue in its effects, but also produces marked irritability, and one gathers that scientific collaboration at high altitudes is apt to be stormy on this account. The fact that residual defect symptoms have not been observed to follow 'gassing' confirms Barcroft's view of the transient effects of non-fatal acute anoxaemia. The so-called neurasthenic symptoms so often seen in men who have been 'gassed' are by no means specific: they are found following a multitude of bodily ailments acquired on active service, and cannot therefore with any certainty be ascribed to the effects of gas-poisoning. Nevertheless, Mott has found multiple small haemorrhages in the brain in fatal cases and we cannot exclude the possibility that recovered cases may also have similar lesions. The residual neuritic symptoms of CO poisoning are well known, but Mott thinks that other factors than simple anoxaemia play a part in their production.

However, although the results of severe anoxaemia are of great interest, it is to mild grades of the condition that particular attention is drawn in the present review, and the phenomena resulting from mild grades belong clearly to more than one category. With hyper-excitability there are unmistakable evidences of impaired efficiency of function. We must also consider the probability that among the positive symptoms will be some that are due to release. There are, therefore, at least three groups of symptoms to be looked for. There is no doubt that impairment of the highest cerebral functions is a constant and early manifestation. Haldane and his co-workers and those who have investigated the reactions of pilots at high altitudes all agree that impairment of judgement, of memory, and of attention are striking features of anoxaemia. Thus, Corbett and Bazett made pilots breathe mixtures with reduced oxygen tensions corresponding to various altitudes from 12,000 to 19,000 feet, and found that their capacity to do simple sums in arithmetic was seriously affected; their answers were inaccurate, often they could not finish the sum, and they were exceedingly slow. Birley reports that at high altitudes perception, memory, and judgement are all affected. Prolonged high flying produces, in addition to these defects, muscular weakness, hypotonus, and inco-ordination, fine tremors, and increased tendon reflexes.

Haldane, Kellas and Kennaway, and Haldane and Poulton found that a rapid fall in oxygen tension in the inspired air caused confusion of mind and twitching of the facial and limb muscles. In their acclimatization experiments the first group of observers found that the earliest noticeable change was diminished perception of light and sound, at a stage when judgement was not yet impaired. At altitudes of about 24,000 feet (reproduced in a steel chamber) there were ataxy and weakness, writing became difficult and almost illegible, the muscles of face and limbs twitched, and all consciousness of the limbs was lost. They were oblivious of the passage of time and could not recall what had passed during the periods spent at these low oxygen pressures. There was inability to calculate, or even to count the pulse, and marked irritability shown as a tendency to violent language and restiveness. They report that 'the general symptoms of anoxaemia were very characteristic, and exemplify clearly certain of the special dangers associated with CO poisoning or high balloon or aeroplane ascents. Thus in the second preliminary experiment J. S. H. became the subject of a fixed idea that it was necessary to remain at 320 mm. Similarly, balloonists usually become possessed at very high altitudes of the fixed idea of going higher, or miners when suffering from carbon monoxide poisoning cannot be diverted from rescue operations, exploring, or fire-fighting work, and often violently resist any one who tries to make them desist. These fixed ideas often take very strange forms. The tendency to singing (observed in J. B. S. H.) and to various forms of uncontrolled emotion is often observed in CO poisoning. Loss of memory was also prominent in the experiments. There appeared to be no real loss of consciousness; but the mental registration of events was quite ineffective, so that a blank remained.'

Any one may reproduce for himself very readily some of the symptoms of anoxaemia, by a two-minute period of rapid forced breathing. This washes carbon dioxide out of the blood and thus renders the oxyhaemoglobin of the blood less readily dissociable. A state of relative anoxaemia results.

Towards the end of the period of forced breathing the hands go into strong interosseal spasm, the arms are extended and pronated, the limbs are pursed and the jaw set, and articulation and mouth opening are difficult. Movements of the arms and hands are unsteady and fine finger movements are lost. The tendon-jerks are increased, the direct and the electrical excitability of the muscles is increased, and there are paraesthesiae of the skin of the trunk and extremities. During the ensuing period of apnoea the paralysis of motion is accentuated. These facts have been known to physiologists for some years and have been recorded by Vernon, Y. Henderson, Douglas, and others. Recently Grant and Goldman have made a detailed investigation of the phenomena, and have pointed out that the symptom-complex of tetany can be produced in this way.

When we attempt to analyse these disorders of function, they seem to belong to at least three groups: (1) defect of the highest cerebral activities, judgement, memory, and attention; (2) release of lower activities from control, manifested in the various emotional symptoms described, and also (3) phenomena of hyper-excitability, of which the muscular twitchings and the irritability are the most obvious expression. It appears that so-called 'irritative' symptoms do not occur alone, but that the discharges from a hyper-excitable centre reveal also severe defects of efficiency in its functioning. For example, the finger movements of a Jacksonian fit are a gross travesty of the finely adapted and co-ordinated movements of which the digits are capable under the influence of the motor cortex, when this is normally activated. In all probability the coarse explosive character of the spinal reflex reactions in man after section of the cord owes its origin to, and is to be explained by, the same mechanism—hyper-excitability and defective efficiency of the spinal centres starved of oxygen.

The presence of the three factors mentioned as responsible for the psychical and purely neurological symptomatology of anoxaemia points to the difficulty there must always be in analysing disorders of function in disease or injury of the nervous system on physiological lines, and warns us to look askance at the deceptive simplicity of the defect and release hypothesis in many of its modern applications.

Fragmentary and incomplete as are the observations we have quoted, and acquired, as they have been, incidentally in the course of investigations directed to other purposes, they give point to the emphasis laid by physiologists upon the extreme sensitiveness of the nervous system to mild degrees of oxygen want. The variety of psychical and somatic neurological symptoms which are produced by this mechanism makes the question one of importance for neurologists. That many of the symptoms of nervous disease and injury arise in this way can scarcely be doubted. Probably all manifestations of what has been called 'irritation', and not a few now attributed to 'release' owe their origin to this cause. However, the hypothesis is not at the moment likely to be received with any enthusiasm, owing to the great swing over of opinion from the time when the fashion was to attribute every positive symptom to some hypothetical source of irritation. The part played by release of function is now better understood, and indeed the tendency is to make excessive demands upon this valuable conception. While not abandoning the earlier hypothesis of 'irritation' and 'release', modern neurology must seriously consider the possibilities of anoxaemia as a very primitive and potent cause of hyper-excitability of nervous tissues. That some very common manifestations of disordered nervous function can justly be attributed to it is made clear by Trotter in the article already referred to. It is by the study of the earliest manifestations of disease and injury of the nervous system, as Mackenzie has so repeatedly emphasized, and not by that of well-established destructive lesions, that we may hope to extend our knowledge of this factor.

It is not our purpose to speculate further upon the many possible applications of this point of view. However, were we disposed to indulge that weakness, epilepsy would at once suggest itself as a fruitful field for the exercise of our ingenuity. This formidable disease has so far resisted all attempts at elucidation, nor do the purely verbal researches and allegorical explanations of the psychogenetic school appear likely to advance our knowledge. Here surely is an instance where investigation should precede speculation unless a promising conception is to be loosely exploited. The sentence quoted earlier from Bayliss, and the study of some recent criminal trials, show that this is no undue apprehension, and we do not want to see the conception of 'cerebral anoxaemia' competing with that of 'buried complexes' as a forensic first line of defence against the legal penalties of some 'irresistible criminal impulse'.

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# ABSTRACTS

## SURGERY

**Bier, A.**, and others. 45. Versammlung der Deutschen Gesellschaft für Chirurgie, 30. März bis 2. April 1921. [**The 45th Conference of the German Surgical Society. (Surgical Tuberculosis.)**] *Deutsche med. Wchnschr.*, 1921, **47**, 489.

The discussion on surgical tuberculosis at the 45th Conference of the German Surgical Society, held in March and April, revealed wide divergencies of opinion as to the most suitable methods for treating surgical tuberculosis. Practically all the speakers subscribed to the importance of heliotherapy, even when this was carried out in the Lowlands, but beyond this there was hardly a single point on which the speakers were unanimous. König, of Würzburg, classified his colleagues according as they preferred: (1) conservative treatment; (2) conservative treatment supplemented, if necessary, by operative treatment; and (3) wholesale operative treatment. He reserved the first class exclusively for Bier, whose conservatism König obviously considered extreme. Pleading for clear-cut principles, he urged the operative removal of foci of disease in the bones, notably when neighbouring joints were threatened. Should such a focus break through into a joint, resection should be performed, and severe mixed infection was an indication for immediate operation.

Defending his conservative standpoint, Bier declared that during the past seven years he had performed only a dozen major operations for tuberculosis of the bones, and that it was of subordinate importance whether sequestra in the neighbourhood of joints were removed or not. Even septic sequestra he had seen absorbed under conservative treatment. His indications for operative interference included only threatening amyloid disease, mixed infection, and the combination of severe pulmonary tuberculosis with severe articular disease. On the other hand, subluxation of the knee was not in itself an indication for resection, and it could be gradually corrected by extension and efficient postural treatment. On the occasions when he abandoned his principle of leaving cold abscesses alone, and aspirated, he did not follow this up with the injection of any fluid. His objection to opening abscesses applied also to those derived from the spine, and he saw no reason for adopting Albee's operation on the spine under any circumstances. The patient's age—over 50—was no excuse for operating forthwith, but he confessed to being driven to amputate in some cases of senile tuberculosis. His three principal remedies were sunlight, passive congestion, and the exhibition of iodine—with these three even very severe cases of surgical tuberculosis could terminate in recovery. In his discussion of the action of sunlight and the significance of pigmentation, he suggested that the benefits obtained were not due to the local action of the sun on the joint, but to a general reaction which enabled the body to mobilize its defences. He combined heliotherapy with carefully graduated passive congestion, and he gave iodine by the mouth as he had found it potent in preventing cold abscesses and the too luxuriant growth of granulation tissue. He had often seen good results from tuberculin in ambulant cases, but his early prejudice in favour of Friedmann's turtle vaccine, containing live, acid-fast bacilli, had not been justified by experience. He also referred to his 'vigorous campaign' against fixation by dressings, and when the lower limbs of his patients were affected he kept them in bed, where they were exposed to the sun, and where, if necessary, appliances for the relief of pressure were used. As soon as pain had ceased, he adopted systematic exercises. With reference to heliotherapy in the Lowlands, he referred to the experiences at Hohenlychen, where the results showed that the success of heliotherapy did not depend on altitude. He raised two other points of interest: under heliotherapy, even severe toxic nephritis may vanish completely, and, as his 18 fatal cases of amyloid disease showed, it is not possible to diagnose this condition before death.

Much of the following discussion resolved itself into an impeachment of Bier's unorthodox views. Garrè, of Bonn, was quite satisfied to dispense with passive congestion and iodine, and, on the other hand, he was favourably impressed by the treatment of cold abscesses with injections of iodoform and glycerine. Open air, sunlight, good feeding, and skin toilette were, in his opinion, the most important factors in the treatment of tuberculosis, and as most of his cases were ambulant, and could not be consistently controlled, he did not, like Bier, dispense with dressings which immobilized the limbs. He had not seen the slightest deformity from the use of plaster of Paris, and he considered the proximity of a sequestrum to a joint, and the persistence of fistulae, as indications for operative treatment. He could not dispense with resections, and he was profoundly sceptical as to the ability of extension alone to correct definite subluxation of the knee-joint. To prevent compression of the cord provoked by abscesses in Pott's disease it was, in his opinion, often necessary to operate.

Referring to the value of actinotherapy, v. Eiselsberg, of Vienna, observed that he made extensive use of quartz light which he had found to be of great value in tuberculosis of the glands. In the case of tuberculosis of the bones and joints he preferred the X-rays. Like other critics of Bier, he considered dressings which immobilized the limbs as essential in ambulant cases, and he considered fistulae, progress of the disease, and multiplicity of tuberculous foci as indications for operative interference. As for resection, he had recourse to it earlier in the case of the knee than in that of the wrist and ankle. He had often noticed that pulmonary foci cleared up after an amputation. His treatment of cold abscesses consisted of incision, evacuation of pus, its replacement by iodoform and glycerine, and careful suture. Only in the late stages of Pott's disease did he consider an operation to be inevitable, and he admitted that the results of laminectomy were disappointing. The beneficial effect of iodine was doubtless due, in some cases, to its action on coincident syphilis. Sauerbruch, of Munich, watered down his praise of heliotherapy with the admission that, in many cases, operative intervention was unavoidable. C. L.

**Ernst, N. P.** Lysbehandling af kirurgisk tuberkulose. [**Actinotherapy of surgical tuberculosis.**] *Hosp.-Tid.*, 1921, **64**, 11–20.

Ernst's survey of the treatment of surgical tuberculosis with the carbon-arc and quartz-mercury lamps at the Finsen Institute in Copenhagen covers a period of seven years. The treatment consisted of exposing the whole body for periods ranging from 30 minutes to 2½ hours every or every other day to arc lamps (75 ampères, 50 volts, or 20 ampères and 50 volts) at a distance of about 1 metre. Eight patients would sit round two large lamps, turning so as to expose every part of the body successively. When the smaller lamps were used, the patients were recumbent, three lamps being suspended between two tables on each of which one patient lay. In the case of superficial lesions, ordinary Finsen light was also employed, and was found to be of considerable value.

The results are tabulated so as to show the number and nature of the various conditions treated, and they are classified according as the lesions were or were not complicated by fistulae or abscesses. There were 141 uncomplicated to 274 complicated cases. All the 23 uncomplicated cases of spina ventosa recovered, the slightest cases after 4–6 weeks' treatment. Only in one of these cases did an abscess form, and it healed quickly after incision. Of the 54 cases of spina ventosa with fistulae, 47 recovered, and several of the failures in the remaining 7 cases were due to such extraneous factors as pneumonia, cancer, insanity, &c. Of 23 uncomplicated cases of tuberculosis of the wrist, 17 recovered with a limitation of movement not exceeding 20°. Among the 29 complicated cases of tuberculosis of the ankle, there were 26 in which the X-rays showed changes; yet, in as many as 11 free mobility, and in 11 others partial mobility, were achieved. During the treatment of these 29 cases, resection had to be performed once, and incision 7 times. Of 40 uncomplicated cases of tuberculosis of the knee, 14 recovered without limitation of movement. All the 42 cases of subcutaneous tuberculosis were complicated; included in this category were 5 cases of anal fistula, and there were probably some in which a bony focus of disease existed. Recovery was effected in 37 of these 42 cases. Uncomplicated tenosynovitis usually proved refractory, 6 out of 7 such cases having to be taken off arc lamp treatment and given X-ray treatment. Yet, curiously enough, 7 out of 8 complicated cases of tenosynovitis responded to arc lamp treatment by recovery.

Taken as a whole, the uncomplicated cases terminated in recovery or improvement in 80 per cent., the complicated in 83 per cent. The percentage of relapses was between 5 and 6 for both groups. As both children and adults were included in these statistics, they do not well bear comparison with the statistics from hospitals devoted only to children or adults. As for the comparative value of the arc lamp and the quartz-mercury lamp, Ernst notes that he has used the latter more and more in recent years, especially for children and slight cases. In 7 cases treatment by the quartz-mercury lamp was replaced by the carbon-arc lamp, but only in one of these was the change followed by definite improvement. A comparison of the results is made with those obtained by Rollier, as published in 1915 in his book on heliotherapy. His results were apparently better in the case of tuberculosis of the ankle, whereas Ernst's were better in the case of tuberculosis of the elbow—a difference suggesting the misleading evidence of statistics based on small figures.

Ernst modifies his advocacy of actinotherapy by including a considerable number of conditions among his contra-indications. They are: fistulae of the shoulder, hip, pelvis, and spine of many years' duration; tuberculosis of the knee in adults when it is evident from the outset that a stiff joint is unavoidable, when subluxation has begun, when the X-rays show great destruction, or when there are large periarticular abscesses. All these conditions are indications for resection. Ernst offers no explanation for the facts that he obtained much better results in complicated than in uncomplicated cases of tenosynovitis, and that the percentage of recoveries was slightly higher among all the complicated than among all the uncomplicated cases. C. L.

**Chievitz, O., Jensen, J., Reyn, A.,** and **Collin, E.** Den kirurgiske Behandling af Knogle- og Ledtuberkulose. [**The surgical treatment of osseous and articular tuberculosis.**] *Hosp.-Tid.*, 1921, **64**, 20–28.

Chievitz's material consists of 233 adults treated in Professor Rovsing's wards and observed for a period of 6–16 years. The object of his analysis was to provide data by which a comparison could be made between the results of operative and other forms of treatment such as actinotherapy. But as many of the cases operated on were severe and had previously failed to react to other treatment elsewhere, this comparison was of limited value. The mortality among 40 cases of hip disease was 28 per cent. (11 deaths all within the first year of treatment). In 17 of these cases, treatment was conservative, being limited to extension which only in one case had subsequently to be supplemented by resection. The mortality among the 65 cases of tuberculosis of the knee was 21 per cent. (14 deaths, of which 10 occurred within 2 years of treatment). Of the 51 survivors, all, with but one exception, were fit for work. Chievitz emphasizes the point that the period of invalidism may be greatly shortened by resection, and 21 of his patients were again at work half a year after the operation. He traces the success of resection in the case of the knee to the fact that all diseased tissue can be discovered and removed—an achievement not always possible in the case of hip resection. The mortality among the 68 cases of spondylitis was 34 per cent. (23 deaths, of which 18 occurred within 3 years of the institution of treatment). Only in 5 cases did new outbreaks of tuberculosis occur, and the fistulae with which 9 patients were discharged ultimately healed except in 2 cases. Of the 7 patients who survived paralyses, 6 ultimately showed no paralysis and were fit for work. Of the 35 patients who exhibited neither abscess formation nor paralysis, only 8 had died. On the other hand, there were 5 deaths among 10 cases of abscess formation, 7 deaths among 15 cases of fistula, and 6 deaths among 13 cases of paralysis. The spinal deformity was not progressive once the disease had become arrested, and the proportion of patients ultimately fit for work was remarkably high; of the survivors only 4 were unfit for work. The treatment adopted was rest in bed, immobilization by Sayre's plaster corset, and aspiration of abscesses. Although some of the patients suffered from multiple tuberculosis, this probably originated from one and the same source and at the same time, in spite of the fact that the clinical manifestations of the disease were not synchronous. In support of this hypothesis, Chievitz notes that in 22 cases with multiple foci, new outbreaks in 16 of these cases occurred within a period of a year. Another fact emerging from these figures is the determination of the patient's fate in most cases within the first few years of treatment; those who survive this by 2 or 3 years seldom succumb to the original tuberculosis or develop new foci of tuberculosis.

Jensen has come to the conclusion that X-ray treatment and light baths have different spheres of usefulness, glandular tuberculosis, as well as tuberculosis of the small bones and joints, being treated most quickly, cheaply, and effectively by the former, whereas the latter is indicated in deep-seated tuberculosis of the large bones and joints, including the pelvis and spine.

Reyn is also an advocate of both methods, but he confesses to disappointment with the results of X-ray treatment of glandular tuberculosis and is sceptical as to the 'brilliant achievements' claimed by German writers,whose publications are apt to deal only with immediate results. The X-rays do, indeed, diminish the size of the glands, but they often fail to return completely to normal. A combination of light baths and X-ray treatment gives far better results and is probably the best extant, except when a single mobile gland can be excised. When tuberculosis of the lymphatic glands is complicated by suppuration and fistulae, this combination may be supplemented with advantage by local Finsen treatment. Reyn's half-hearted advocacy of X-ray treatment is the outcome of many years' experience, during which he has treated several hundred cases in many different ways. He cannot dismiss inhibition of growth by X-ray treatment as a fantasy, for in the case of a child treated for lupus with the X-rays he has seen permanent inhibition of development on one side of the lower jaw. The development of the teeth on the same side was also inhibited, and the face was very asymmetrical. The ultimate results of deep X-ray treatment are uncertain, and there are probably many unpleasant surprises to be disclosed some years hence. Already Reyn has seen atrophic changes with dilatation of the cutaneous blood-vessels developing long after the cessation of X-ray treatment of patients who, at the time, showed no reaction. In this connexion, it is probably dangerous to push X-ray treatment of spina ventosa in children. In contrast to his rather gloomy views on X-ray treatment, Reyn is emphatic in his advocacy of universal exposure to light baths. Before the adoption of this treatment at the Finsen Institute in Copenhagen, amyloid disease was not very rare in cases of lupus; now, however, it is practically never seen, the universal light baths apparently counteracting all the injurious effects of chronic suppuration.

Collin's study of cases of surgical tuberculosis treated at the Rigshospital and the Finsen Institute during the past five years has led him to distinguish between osseous and synovial disease in estimating the comparative merits of X-ray treatment and light baths. He finds that synovial tuberculosis reacts best to the X-rays, whereas it is the form of tuberculosis which is least amenable to treatment with light baths. Osseous tuberculosis, on the other hand, may improve under, but is seldom cured by, the X-rays, which are definitely inferior in this respect to light baths. C. L.

**Maalöe, C. U.** Om den praktiske Værdi af Gastroskopi ad modum Elsner. [**The practical value of Elsner's gastroscopy.**] *Ugesk. f. Læger.*, 1921, **83**, 525–35.

Since August 1912, Maalöe has made 470 examinations with Elsner's gastroscope without a single disaster. In 36 cases he could not introduce the instrument into the stomach for various reasons, a frequent obstacle being the diaphragm. In 58 other cases a complete view of the stomach could not be obtained, although the gastroscope was successfully passed into the stomach. In 213 cases the stomach was seen to be normal, and with increasing experience Maalöe has come to attach great importance to such a negative finding. It was confirmed in numerous cases by the X-rays or the subsequent course of the case, and in 17 cases by operation. His 17 diagnoses of cancer were all confirmed, 12 by operation and 5 by the subsequent course of the case. In 5 cases he was misled by the gastroscope, and in 2 of these cases ulcers near the cardiac end of the stomach, which is least accessible to gastroscopic examination, were overlooked. Ulcers were found in 95 cases, which were classified according as they were juxta-pyloric or supra-pyloric. In 38 out of the 47 cases of juxta-pyloric ulceration, the gastroscopic diagnosis was confirmed by operation; this in 2 cases showed that a stenosis observed by gastroscopy was probably only spasmodic. In 16 cases in this group an operation was undertaken chiefly on the evidence of gastroscopy. Supra-pyloric ulceration, of which there were 48 cases, is the condition which, more than any other, justifies gastroscopy. In 35 cases the diagnosis was confirmed by operation, and in 10 others there could be no doubt as to the correctness of the diagnosis. By indicating not only the existence, but also the exact position and character of a supra-pyloric ulcer, gastroscopy gives certainty to the diagnosis of a condition about which other diagnostic methods yield comparatively little exact information. Maalöe's advocacy of the gastroscope concludes with a plea for its use in controlling the results of operative treatment. He calculates that in about a quarter of all cases of gastric ulcer the diagnosis cannot be made without the help of the gastroscope, which is an invaluable aid to distinguishing between nervous dyspepsia and actual ulceration. C. L.

**Müller, S.** Enterostomi ved postoperativ Ileus. [**Enterostomy for post-operative intestinal obstruction.**] *Hosp.-Tid.*, 1921, **64**, 11–18.

Müller argues from eight cases of acute appendicitis with post-operative intestinal obstruction treated by enterostomy, and from the literature of the subject, that this step may, under certain conditions, save the patient's life. Post-operative intestinal obstruction which occurs as late as the third week after the operation is usually due to some mechanical obstruction and not to paralysis of the gut. But during the first two weeks it is difficult to decide whether intestinal obstruction is due to mechanical or 'dynamic' causes. The differential diagnosis may be almost impossible without exploration. Thus, in one case, a man aged 25, was operated on for acute appendicitis on the fourth day of the disease. Purulent peritonitis with partial gangrene of the appendix was found. A drain was inserted into the pelvis. Flatus passed on the second day, faeces on the fourth. But, in spite of daily evacuations, there was progressive abdominal distension with vomiting. Enterostomy was performed on the eleventh day, by which date the partial intestinal obstruction had become complete. It was thought that the symptoms were due to extension of the peritonitis, but when the abdomen was opened in the middle line, no peritonitis was found; the distended and injected small intestine floated in clear fluid, the condition resembling that of intestinal obstruction due to some purely mechanical cause. Enterostomy gave great relief, and five days later there was evacuation by the rectum, and the patient ultimately recovered.

On the other hand, in another case, there was no free peritonitis when the patient was operated on for acute appendicitis after two days' illness. The appendix was thickened, and its mucous lining ulcerated and partially gangrenous. It was shelled out from its bed in the caecum, to which it was attached by adhesions. Enterostomy was performed on the eleventh day for acute intestinal obstruction, and, to Müller's great surprise, severe fibrino-purulent peritonitis was found. The patient died next day. After contrasting these cases to emphasize the difficulties of distinguishing between mechanical and 'dynamic' intestinal obstruction, Müller suggests that post-operative intestinal obstruction is usually due to a combination of these factors.

Five of Müller's eight patients recovered. Enterostomy was performed within eleven days of the original operation in every case and was not undertaken till other mechanical and medicinal remedies had been given a fair trial for several days. Müller's results compare favourably with Giertz's. In 1907 the latter published sixteen cases of post-operative intestinal obstruction, in only two of which enterostomy proved beneficial. As the material in these two series was approximately identical, the differences in the results may be sought in differences of technique. The level at which the gut is opened may play a certain part in the further course of the case, but of greater importance is keeping the enterostomy opening small. An opening which grows to a width of 4 to 5 cm. and comes to act as an artificial anus, as in Giertz's experience, is far less satisfactory than the opening which just admits a small Pezzer catheter, as used by Müller. In all his five cases terminating in recovery the enterostomy opening closed spontaneously. Even in the three cases which terminated fatally from peritonitis the enterostomy gave marked relief from such distressing symptoms as vomiting. In three cases the cause of the obstruction was chiefly mechanical. Of the five cases in which the cause of the obstruction was mainly 'dynamic' (extensive peritonitis) two terminated in recovery.

C. L.

## NEUROLOGY

**Jeliffe, S. E. Multiple sclerosis and psycho-analysis.** *Am. J. M. Sc.*, 1921, **161**, 666.

Flushed with its triumphs in the realms of the psychoneuroses, clinical psychology is now boldly attacking the problems of organic disease. Epilepsy has for some time been studied from this point of view, though it has not yet yielded up its secret to the interviewers. Recently, it has been stated that the pernicious vomiting of pregnancy is purely hysterical in origin, while during the present year a writer in the *British Medical Journal* has quoted and described two cases of hysterical fits in support of the contention that Jacksonian epilepsy may be of psychogenic origin. In the latter instance, of course, the argument would have been more convincing had there been no doubt about their Jacksonian character.

It is now the turn of multiple sclerosis to be subjected to what may be called a journalistic method of scrutiny. Jeliffe describes his paper as 'a preliminary statement of a tentative research', and, as though appalled by the dreadful lucidity of the phrase, plunges at once into a veritable maze of obscure and involved phraseology, of which the reader will vainly seek to discover the meaning. In many places, indeed, the reviewer has been so utterly baffled in his endeavour to understand and to summarize the argument, that it has been necessary to resort to somewhat fuller quotation than is generally desirable in a review.

According to Jeliffe there are primary and secondary types of multiple sclerosis. The secondary type, which he excludes from his research, consists of cases which he regards as of varying aetiology and mainly infective in origin. The clinical picture is that of multiple sclerosis; the lesions are disseminated throughout the nervous system, and should the spirochaete now being investigated by Kühn and Steiner and others prove specific for the disease, all cases so caused will belong to the secondary type. Having thus ruthlessly cleared all obstacles from the path of his hypothesis—and there seems no other justification for excluding all these cases—Jeliffe proceeds to discuss a so-called primary type. 'Here the chief pathological lesion seems to have its inception in a special type of disturbance of the vascular apparatus which is functionally integrated with the work being carried on in the different neural metameres.' This lesion 'shows certain affiliations with another type of vascular alteration . . . the exudative diathesis'. Apparently angioneurotic oedema, asthma, and other similar conditions are intended here. He continues that 'the argument briefly stated is that in a certain type of "multiple sclerosis" patients certain vascular reactions occur which permit exudative and proliferative changes of a nature similar to those seen in certain constitutional states known to be intimately related to vegetative nervous system disorders of a special type'. The object of the research has been 'to determine the relationships of these phenomena to vegetative nervous system control and attendant psychological factors', and further to form the basis of a general attack upon the problems of nervous disease, and indeed to formulate a general dynamic pathology. With this clear expression of his point of view, Jeliffe passes on to what he states are physiological considerations. This section of his paper shows a strong similarity to the recently reviewed paper of Pierce Clark (*Medical Science*, 1920, **3**, 56) on the psychogenic origin of epilepsy, in that although the vocabulary is physiological, for we read of postural tonus, of proprioceptive nerve-supply, and of neural integration, yet the use of the terms is totally foreign to physiology, as are also the conceptions they are intended to illuminate. It seems possible that this section of the paper is, to use a favourite conception of the author, purely symbolic, and that the meaning of the symbolism has escaped the reviewer.

Briefly, Jeliffe's conception of disseminated sclerosis is based upon the psycho-analysis of five patients said to be suffering from this disease. The dream content of these individuals showed constantly an archaic form of symbolism, which Jeliffe, in accordance with his often stated views on psychic symbolism, regards as indicating either regression or the non-attainment of a high level of psychic symbolism. The result is a restricted outlet for the affect, or feelings, which are, therefore, discharged downwards into the somatic pathways of the nervous system. These, being already in full activity, are overloaded with energy and are wrecked, so that exudative and proliferative changes take place and multiple sclerosis is produced. The abnormally diverted affect, he says, 'is dragging at the personality and forcing it into separateness from the world in the fantasies of a psychosis, or it is allowing its destructive activities on some somatic pathway as in these multiple sclerosis cases'. This he calls 'looking at the situation from the point of view of making the body the scapegoat of the spirit'. The reviewer would prefer to regard the whole hypothesis as an example of making the intelligence the catspaw of the imagination.

Hypotheses of the kind clearly do not come within the scope of ordinary criticism and analysis. Indeed, they merely excite bewilderment, mirth, and finally despair, until the reader's somatic pathways stand in grave danger of being wrecked. One's first impression is that the paper is intended as a satire on the psychogenetic school of thought, somewhat on the lines of Archbishop Whately's famous pamphlet 'Historic Doubts relative to Napoleon Buonaparte'. As one reads on, however, it becomes clear that the paper is really what it purports to be, namely, 'a preliminary statement of a tentative research.' F. M. R. W.

**Stertz, G.** Die funktionelle Organisation des extrapyramidalen Systems und der Prädilektionstypus der Pyramidenlähmung. [**The organization of the extrapyramidal motor system and the selective incidence of paralyses of pyramidal origin.**] *Ztschr. f. Nervenheilk.*, 1921, **68-9**, 481.

The author attempts to explain the occurrence of compensation after pyramidal tract lesions in terms of the extrapyramidal motor systems. He draws up the following tables in which the results of pyramidal and extrapyramidal lesions are compared. Pyramidal lesions result in an initial loss of voluntary power with persistent loss of skilled isolated movements; in the development of involuntary mass movements—associated movements; in increased peripheral reflex excitability leading to reflex spasms in certain muscle groups, but not in others; in the appearance of the Babinski type of plantar response: in the development of flexion contracture of the upper limb and extension contracture of the lower limb; and in predominant affection of the distal segments of the limbs. On the other hand, extrapyramidal lesions result in retention of voluntary power and of skilled movements; in slowness of muscular contraction and relaxation leading to the adoption of fixed attitudes and general poverty of movement; in the absence of reflex changes.

He supposes that the motor cortex and its projection tract subserve voluntary power and particularly the performance of the skilled purposive movements of the individual, while they also inhibit lower level reflex mechanisms. The extrapyramidal system, on the other hand, is the organ by which impulses descending from the cerebellum to maintain and to modify posture and tonus are regulated. It is a reflex mechanism showing reciprocal innervation. Increased activity of this reflex leads to the production of the amyostatic syndrome (that is, the paralysis agitans syndrome) (*Medical Science*, 1920, **2**, 180). Restoration of motor function after pyramidal lesions depends upon the fact that the vital movement complexes, such as sucking, deglutition, and posture, are represented in subcortical motor centres, to which, when the true motor cortex is out of action, the ascending stream of peripheral impulses is diverted. They are thus caused to overact, a state of affairs aggravated by the removal of cortical control. These centres are innervated voluntarily by the action of intact non-motor regions of the cortex.

Here, as in other recent continental papers, it is interesting to watch the gradual approximation to the views held in this country on the problems of motor co-ordination. It may, however, be permitted to add that continental writers have not yet fully appreciated the recent advances which have been made in this country on the physiology of the nervous system, and cling to old and fantastic conceptions that will not bear analysis in the light of modern physiological knowledge. Thus, while it is clear that Stertz appreciates the striking clinical differences between the positive symptoms of pyramidal and extrapyramidal lesions respectively, and realizes that release of function accounts for the former, yet he at once proceeds to confuse the two by attributing the amyostatic syndrome to a heightened activity of the postural reflex mechanism. With this it clearly has nothing to do; it depends upon an as yet uncomprehended disorder of some other element in the complex system of extrapyramidal paths.

Possibly, much confusion arises from a lack of appreciation of the true functions of the cerebral motor cortex, as they have been elucidated by Sherrington and Leyton (*Medical Science,* 1921, **3**, 349). Co-ordination, in the simple sense of the word, is not a function of the motor cortex. The reflex reactions of the decerebrate and spinal animals are perfectly co-ordinated. They consist in relatively simple large movements employing all the skeletal musculature of the body for the maintenance of posture and its suitable modification, and for defensive, sexual, nutritive, and locomotor reactions. In other words, motor co-ordination is represented in the bulbo-spinal levels. The function of the motor cortex is to analyse these large and simple movements, to pick out from them such fractional elements as are needed for voluntary purposive movements, and to combine them into an infinite variety of combinations and sequences, which represent the normal voluntary motor activities of the individual. Hence destruction of the motor cortex or of its projection tract produces loss of voluntary power, and release of lower level reflex mechanisms, which can still under appropriate stimulation produce the simple reactions we have described. On the other hand, lesions interfering with any of these lower level mechanisms necessarily disturb co-ordination, though not voluntary power, because the lower centres upon which the motor cortex now plays are defective. Therefore, extrapyramidal diseases are characterized not by paralysis, but by disorder of movement. Further, these disorders do not indicate that now cortical innervation is excessive, because, as is often stated, some controlling influence is removed. Clearly, the conception of release has no place here, for the reflex mechanisms in question are subordinate to the cortex. The disorders of co-ordination and of tone resulting from cerebellar lesions in man may be readily interpreted from this point of view. Postural tonus, an essential element in co-ordination, is destroyed and ataxy necessarily results. However, it must be admitted that many neurologists would object to regard atonia as directly responsible for ataxy—largely because the idea is so simple and threatens to tear away much of the delightful mystery surrounding cerebellar functions. The fact recorded by Luciani that an animal after extirpation of its cerebellum does not show inco-ordination when it is swimming seems to indicate that the fixation or resistance provided by postural tonus may be reproduced in a measure by movement in such a resistant medium as water, and lends support to the view regarding atonia as causing ataxy. The problem of the amyostatic syndrome is much more difficult. The rigidity of this is not a mere increase of normal tonus, and thus it is not comparable with the hypertonus of pyramidal tract lesions.

Förster states that the rigidity of paralysis agitans, the most familiar example of the amyostatic syndrome, is not abolished by posterior root section—that is, by de-afferentation. Therefore, it must be something very different from tonus and hypertonus as we know them. At the moment its physiological interpretation is quite obscure, and so purposeless does it appear that one is tempted, despite the objections such a view will provoke from those who regard release of function as an adequate explanation of all positive symptoms, to regard it as inherently pathological and due to perverted activity of some unknown motor mechanism in the region of the basal ganglia. The source of the tremor which so often accompanies it and the relation of the two, if there be any, are also quite unknown. They seem likely to remain so as long as we continue to assume that hyper-excitability and hypo-excitability, excess and defect, are the only ways in which the nervous system can react to disease and injury, and that aberrant activity involving no question of release of function cannot and does not occur. Surely, the coarse travesty of activity shown by the motor cortex in a Jacksonian fit is sufficient to indicate that function may vary qualitatively as well as simply quantitatively. F. M. R. W.

**Neal, H. V. Nerve and plasmodesma.** *J. Comp. Neurol.*, 1921, **33**, 65.

The author quotes Ross Harrison as saying that 'the work on the cultivation of tissues may be said without reserve to have completely proved the correctness of the conception of His and Ramon y Cajal' in favour of the cell process of neurogenesis as opposed to the cell-chain hypothesis. However, many problems remain unsolved, such as that of the genesis of nerve-sheaths and of sympathetic cells. One of the remaining points of dispute is whether or not there exists previous to neurofibrillar connexion between neural tube and myotome a connexion by means of undifferentiated protoplasmic threads or plasmodesmata. Even admitting the existence of these, it is not certain whether they are primary—the result of incomplete cell division—or secondary—the result of protoplasmic outflow of medullary cells. Even allowing that they are secondary, it is not agreed whether indifferent glia cells or medullary neuroblasts first link nerve and muscle.

If we adopt Apathy's dictum that only the presence of neurofibrillae indicate the nervous nature of tissue, we shall be prevented from regarding as a primitive nerve all cellular strands extending between nervous system and muscle.

The present paper raises three disputed questions; namely, are the connexions between muscle and nerve primary or secondary; are neuro-muscular connexions primarily undifferentiated plasmodesmata, or are they neurofibrillar; are neuromuscular connexions effected by indifferent cells or by neuroblasts?

Neal answers these questions as follows: In embryos of *Squalus acanthias* previous to the stage of 4·5 mm. there is no primary connexion between neural tube and myotome, protoplasmic connexion is made later and secondarily. (2) Outgrowths of neuroblasts in the neural tube then make connexion with the myotome and within these outgrowths neurofibrillae soon make their appearance. Hence the neuromuscular connexion is truly neural—that is, the plasmodesmata are nervous structures.

(3) Although indifferent elements may be associated with the plasmodesmata, yet these are secondary and do not themselves make the neuromuscular junction.

In conclusion, since the neuromuscular connexion is nervous *ab initio*, the use of the term plasmodesma seems unnecessary. F. M. R. W.

**Cassirer, R.**, u. **Lewy, F. H.** Zwei Fälle von flachen Hirntumoren. [**Two cases of superficial brain tumour.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1920, **51**, 119.

This paper is a contribution to the subject of 'pseudotumour', a condition in which the clinical picture is that of cerebral tumour, but in which recovery occurs, or, in the event of death, no tumour is discovered.

The authors consider that Reichardt's theories and Alzheimer's discovery of amoeboid glia cells fall short of a full explanation of the condition. They report two cases of apparent 'pseudotumour' and discuss their bearing on the problem.

The first was that of a middle-aged woman with left abducens paralysis, severe optic neuritis more marked on the left side, a tendency to fall to the left, and tenderness of the skull over the posterior fossa of the skull. Decompression did not relieve the symptoms and at autopsy an apparent encephalitis in the region of the left angular gyrus was found. Microscopical examination revealed a diffuse sarcomatosis of the vessels entering the cortex of the left angular gyrus, and the left inferior surface of the cerebellum. There were also numerous amoeboid glia cells and an increase of glia fibrils under the ependyma of the left lateral ventricle in the neighbourhood of the corpus callosum.

The second case was that of a man of thirty, who had headache, vomiting, optic neuritis, and also attacks of loss of consciousness attended with stertorous breathing and slowing of the pulse. There were various cranial nerve palsies, tendon arreflexia, and blindness ensued within a few months of the onset of symptoms.

Autopsy revealed no naked-eye tumour, but microscopically the pia over frontal and parietal lobes was infiltrated with typical round cells of sarcomatous nature.

In both cases there were numerous minute growths, which appeared to have arisen in the adventitial lymph spaces. Blockage of these they regard as causing oedema of the brain and glia cell proliferation. Lumbar puncture was not performed in either case. Rindfleisch's meningitis sarcomatosa is comparable with this condition. They conclude that lumbar puncture might well have a great diagnostic value in cases of 'pseudotumour', on account of the possible cellular content of the fluid in cases such as those now reported.

They consider that 'pseudotumour' should never be diagnosed without careful microscopical examination of the brain. H. W. H.

**Johnson, S. E.**, and **Mason, M. L.** **The first thoracic white ramus communicans in man.** *J. Comp. Neurol.*, 1921, **33**, 77.

The text-books of anatomy are not explicit nor in accord as to the existence of a white ramus communicans in connexion with the first thoracic spinal nerve. The authors find that in each of twelve subjects examined, one or more white rami arise from the first thoracic nerve and run as a rule to the stellate ganglion. They contain a relatively high percentage of large medullated fibres. The inferior cervical and the first thoracic sympathetic ganglion are commonly, but not constantly, fused. Rami from the eighth cervical nerve are neither white nor mixed in character, and the condition described above is to be regarded as the rule in man. F. M. R. W.

**Lloyd, J. H. Syphilis of the eighth nerve.** *Arch. Neurol. & Psychiat.*, 1921, **5**, 572.

Hendrie Lloyd gives the characteristics of syphilis of the eighth nerve as follows: (1) Onset may occur early in the secondary stage. (2) Onset may be sudden and rapid, so that the patient may become deaf in a few days. It may be accompanied by tinnitus, which is marked and distressing. (3) It is usually bilateral. (4) It may be part of a cranial polyneuritis; the seventh nerve is most commonly involved, but the second, third, and fifth may also be affected. The pathological basis of the condition is a basilar syphilitic meningitis, and headache and a lymphocytosis of the cerebrospinal fluid may be present. (5) The two divisions of the nerve may be unequally affected, the cochlear in one case and the vestibular in the other bearing the brunt of the disease. (6) The condition may be persistent and incurable. F. M. R. W.

**Jacobi, W.** Über psychische Störungen bei Basalgangliengeschwülsten. [**Mental disturbances in tumours of the basal ganglia.**] *Monatschr. f. Psychiat. u. Neurol.*, 1921, **49**, 3.

In 1902, Schuster collected reports of a series of 54 cases of tumour of the basal ganglia, in which mental disorders were recorded, and concluded that in no case was the psychical disorder of localizing significance. Pfeifer reported three cases of basal ganglia lesion with the Korsakow syndrome, and others with convulsive manifestations, but he also could not conclude that these symptoms possessed any localizing value. The mental inertia, forgetfulness, and somnolence described by Veronese as characteristic of tumours in this region, Pfeifer refers to the general rise of intracranial tension associated with any intracranial tumour. Various manifestations of a psychical nature have been recorded by different writers, but neither their occurrence nor their form are constant or characteristic, and Redlich, Bruns, and Oppenheim have insisted that tumours in this region may run their course without any evidence of mental disturbance.

Jacobi reports three personally observed cases, but in each of them there is evidence of such severe compression of the brain, from direct pressure of the growth and from secondary internal hydrocephalus, that they are useless as physiological material, and no one would care to draw conclusions as to the localization of psychical disorders from them.

H. W. H.

**Kirby, G. H., and Davis, T. K. Psychiatric aspects of epidemic encephalitis.** *Arch. Neurol. & Psychiat.*, 1921, **5**, 491.

From the study of eighteen cases with mental disorders, the authors reach the following conclusions. The psychical disturbances of epidemic encephalitis resemble those of a toxic-infective psychosis. In the acute stages of the disease, torpor and delirium are the common mental disorders, although other clinical pictures may be observed, such as the Korsakow syndrome.

The disturbances of sleep may be in the nature of hypersomnia-drowsiness, lethargy, and stupor, or hyposomnia. The patient tends to be sleepless by night and somnolent by day. A great majority of patients show delirium at some stage of their illness. The content of this tends to circle round habitual trains of thought and occupation of the patient. Before its onset changes of mood and disposition are often seen, and a state of euphoria may ensue after its passage. On the other hand various grades of depressive reaction may follow the delirium. During the lethargy, some emotional response can be obtained to an adequate stimulus. In all unrecovered cases, some change in disposition remains and may be the only sign of incomplete recovery. F. M. R. W.

**Redlich, E.** Zur Pathologie der Epilepsie nach Schädelschussverletzungen. [**On the pathology of epilepsy following gun-shot wounds of the skull.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1919, **48**, 8.

Redlich, in an article of 110 pages, gives a critical account of 57 cases of epilepsy occurring in patients with gun-shot wounds of the skull. There is a good bibliography and many running references in the text, rendering the article representative of Austro-German thought on this subject. Of the 57 cases, 18 are classified as early epilepsy, 39 as late epilepsy.

The earliest attack in the latter class was at the end of two months. Of the 57 cases on which this study is based, 33 had an outspoken paralysis. Attacks of the Jacksonian type were the most common, but they often went on to complete unconsciousness. An aura was frequently present, often of long enough duration to allow of the subject making preparation for the attack. As to the part primarily affected by the convulsion, Redlich has precise information in 27 cases. Of these, the upper extremity led the attack in 16 cases, the lower extremity in 4, the face and the body once each, and the site of onset was variable in 5. He compares these figures with those of Heinrich Braun: arm 47, leg 7, face 18. In the cases where the arm was first convulsed, the thumb generally led, and next the fourth and fifth digits. The convulsion may begin in a part which is not severely injured, e. g. with a severe palsy of the hand the attack may often originate in the elbow or shoulder. Kirschner has pointed out that a part of the central convolution may be so severely damaged that it is no longer an epileptic centre, but the interference with the blood and lymph circulation may be so embarrassed as to convert the neighbouring motor cortex into an 'epileptogenic zone'. Krause concurs in this opinion. One must suppose that there is a motor focus which is the starting-point of the convulsion and that it is necessary that its ganglion cells and association fibres be intact in order that it may originate an attack. However, paralysed limbs do actually take part in the fits, but Redlich thinks that the muscles do not contract in a discrete manner. Temporary aggravation of paralysis and sometimes aphasia follow the attacks, these phenomena being of the nature of exhaustion palsies. Sudden attacks of weakness in a limb, such as a sudden and temporary inability to perform a movement, the author regards as 'paralytic equivalents' of Jacksonian attacks. Although Jacksonian epilepsy was the common type of seizure, a few cases presented ordinary generalized attacks. But petit mal, faints, and dizziness were not common, probably because the wounds in this series so often overlay the motor area. The Austro-German statistics available show that parietal wounds lead to fits more often than wounds elsewhere on the skull. In Redlich's cases 63·7 per cent. of the injuries were parietal in situation, but in 45·3 per cent. of non-epileptic head wounds the injuries were also parietal. One concludes that the situation of the wound is of secondary and not of primary importance. As to the influence of a defect in the skull, 63 per cent. had a pulsating defect, 10 per cent. had a defect which did not pulsate, and 19 per cent. had no discoverable defect. No conclusion can therefore be drawn from this. The author points out, as many others have done, that the closure of a defect may lead to epileptic seizures. The like may follow operations on wounds of the brain remote from the motor area. On the whole, the epileptic attacks are relatively infrequent. Rarely one single fit has occurred and then no more: 4 cases—one early, and the others 15, 18, and 26 months after injury.

In only 8 of 29 fully investigated cases was there any family taint which might have predisposed to epilepsy.

Examination of the vascular system and of the cerebrospinal fluid leads to some interesting points. Bradycardia was common, often below 60, but varying with posture. The blood-pressure tended to be low (usually below 130 mm. Hg). A leucocytosis was present in the greater number of cases after an epileptic seizure and lasted several hours. The blood is best examined within 6 hours of the fit. A typical example showed 16,500 white cells after 5 hours, 10,300 after 8 to 10 hours, and 8,000 after 10 hours. This leucocytosis is especially found in cases with generalized convulsions, whether beginning as a focal fit or not. It has been found in pure Jacksonian attacks, and once after a faint only. Redlich's experience has not been large enough to enable him to draw any very decided conclusions, but he hazards the view that a protein intoxication closely resembles in its blood picture these epileptic cases. No particular change was found in the cerebrospinal fluid. The pressure was usually low. In 26 cases it was normal in 9 (120–150 mm. of water), in 8 it was 150–180 mm., in 5 180–200, and in 4 it was over 200 mm. This combats Kocher's view that there is constantly an increased cerebrospinal fluid tension in these cases.

Splinters of bone or metal were found in 33·6 per cent. of the epileptic cases, and in 21·6 per cent. of the non-epileptic. To such foreign bodies the causation of epilepsy cannot be assigned. Nor does Redlich think that the causal relationship of brain adhesion and dragging on the scar at each cerebral pulsation as a factor in epilepsy is proven. Nevertheless, he considers that the therapeusis of epilepsy is essentially surgical. German thought seems to favour a revision of the wound area and fascial reconstitution of the dura. Finsterer recommends the use of hernial sac to replace the destroyed lepto-meninges.

Opinion is divided as to the efficiency of closing the bone defect in these cases. Redlich, after discussing the various methods in vogue, concludes 'In any case the number of cases which have been cured of epilepsy by closing their defects is so small, the theoretical objections to this manœuvre so great, that at the present time closure alone cannot be recommended as an efficacious proceeding for the operative treatment of epilepsy following gun-shot wounds'.

Many of Redlich's cases have been operated upon by different surgeons, but in no case was there a recovery which looked like being permanent. On the other hand, drugs were equally unavailing.

The paper is a valuable contribution, but is badly arranged and not easy to read. It concludes with a detailed account of thirteen of the more interesting cases. G. J.

## PATHOLOGY AND BACTERIOLOGY

**Caldarola, P.** Ricerche sierologiche sui meningococchi, parameningococchi e gonococchi [B]. [**Serological investigations on meningococci, parameningococci and gonococci.**] *Ann. d'ig.*, 1920, **30**, 7 and 108.

The following conclusions were reached: (1) Both the agglutination and the Bordet-Gengou reaction are sufficient for the bacteriological diagnosis of a meningococcal infection. The two reactions lead to analogous results, but the former is to be preferred for practical purposes because of its simpler and quicker execution. If agglutination is carried out with sera corresponding to known varieties of meningococcus, it is, as a rule, possible to identify by this means the strain under investigation, because, all other conditions being the same, every strain is agglutinated in dilutions greater in the case of a homologous than in that of a heterologous serum. (2) The various strains, besides being agglutinable in different degrees, have also different antigenic power, so that sera of only a low agglutinating power are obtained by the immunization of animals with certain strains. (3) The existence of serologically distinguishable types of meningococci cannot be questioned any longer, but this does not justify the use of the terms 'meningococci' and 'parameningococci', because amongst the various types there are not such cultural and biological differences as, for instance, between *B. typhosus* and *B. paratyphosus*. (4) The slight group reactions between antimeningococcal sera and gonococci, or, vice versa, between antigonococcal sera and meningococci show that a great affinity exists between these two groups of micro-organisms, but they do not justify the paradoxical supposition that gonococcus and meningococcus are the same germ differentiated into two pathogenic entities due to their localization in different organs. (5) The group reactions between antimeningococcal sera of Nicolle's type and certain strains of meningococci are rather remarkable; sera obtained by means of the latter may, in their turn, give positive group reactions with other varieties of meningococci, the sera of which remain inactive with heterologous strains in cross tests. Such strains must therefore represent intermediate varieties between Nicolle's types. This may explain why the classifications of different authors (Dopter, Gordon, Nicolle) do not entirely correspond with one another. (6) It may be assumed that the meningococcal protein, fundamentally the same, may become, through unknown factors, modified in such a way as to give origin to different pathogenic varieties, the predominance of each of which imparts to each epidemic its peculiar character. But besides the predominant groups there must be strains of meningococci which do not correspond to any of the known types and can be considered as transitional varieties. (7) For these various reasons it appears advisable from a practical point of view to use polyvalent sera for the treatment of all cases of meningococcal infection, either not

bacteriologically ascertainable, or not yet serologically identified. But whenever and as soon as the prevalent meningococcal type has been recognized, resort should be made to the corresponding monovalent serum.
C. d. F.

**Weinberg, M.**, et **Otelesco, I.** *B. proteus* des plaies de guerre. [**B. proteus of war wounds.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 535.

This is a short account of 8 races of *B. proteus* isolated from war wounds. With one exception all were able to produce indol. All produced a haemolysin. In doses of 1 to 5 c.c. injected subcutaneously or into the muscles of guinea-pigs death occurred, sometimes actually in a few hours, with intense sanguinolent oedema, which was occasionally gaseous. In all the fatal cases in animals the microbe was found in the blood. The association of *B. proteus* with *B. perfringens, V. septique, B. oedematiens, B. fallax, B. histolyticus*, and *B. bifermentans* enhances the virulence of the anaerobes. The proteolytic properties of *B. sporogenes, B. bifermentans*, and *B. putrificus* are arrested *in vivo* by cultures of *B. proteus*. Although, as it is well known, *B. sporogenes* in association with pathogenic anaerobes provokes the lesions of gas gangrene in guinea-pigs, this is not so when it is mixed with small quantities of *B. proteus*. In the latter case the lesion is not gangrenous. Normal sera, especially that of the horse, manifests definite antihaemolytic properties against proteus haemolysin. W. B.

**Blanc, G.** Recherches expérimentales sur le virus de l'herpès. [**Researches on the virus of herpes.**] *Compt. rend. Acad. d. Sc.*, 1921, **172**, 725.

Blanc, working at the Pasteur Institute of Athens, repeated and extended the experiments of Lowenstein, Doerr, and others, on the virus of keratitis herpetica, which produces in rabbits a keratitis capable of being transmitted in series. Blanc confirms this work and finds that by infecting the cornea of a rabbit with the contents of a herpetic vesicle a typical local lesion can be produced, characterized by keratitis, herpes of the cornea, and a purulent conjunctivitis. Intradural injection of the material obtained from a human case of herpes, whatever its cause, or from the keratitis of the rabbit, produces an encephalitis which kills the rabbit in about five days. The encephalitis can be reproduced in series by using emulsions of brain. In the rabbit considerable restlessness, convulsions, and periods of lethargy characterize the disease. The virus is filterable, and no organism can be demonstrated or cultivated by the usual methods. Blanc points out the close resemblance which exists in the experimental animal between the encephalitis of herpetic origin and that due to the virus of encephalitis lethargica. J. R. P.

[Recent experimental work on this interesting condition will be found in the following papers:

**Löwenstein, A.**, *Klin. Monatsbl. f. Augenh.*, 1920, **64**, 15.
**Doerr, R.**, ,, ,, ,, 1920, **65**, 104.
**Stoker**, ,, ,, ,, 1920, **65**, 298.
**Kraupa**, *München. med. Wchnschr.*, 1920, **67**, 1236.
**Luger** u. **Lauda**, *Wien. klin. Wchnschr.*, 1921, **34**, 132.
**Blanc, G.**, et **Caminopetros, J.**, *Compt. rend. Soc. de biol.*, 1921, **84**, 629.

W. B.]

**Volpino, G.**, e **Desderi, P.** Osservazioni microscopiche sopra i cervelli in alcuni casi di encefalite epidemica. [**Microscopic observations on the brains from some cases of epidemic encephalitis.**] *Ann. d'ig.*, 1920, **30**, 81.

**Gamma, G.** Sopra uno speciale reperto microscopico che si osserva nel tessuto nervoso degli ammalati di encefalite letargica. [**On a special microscopic finding in the nervous tissue from cases of lethargic encephalitis.**] *Gior. d. r. Accad. di med. di Torino*, 1920, **83**, 123.

The investigations of Volpino and Desderi were made on pieces of brain from five cases of epidemic (lethargic) encephalitis dead between 9 and 30 days after the onset of the disease. Material was fixed in Zenker's fluid, 10 per cent. formol, and a mixture of alcohol, mercuric chloride and acetic acid, and then embedded in paraffin. In sections 5 to 10$\mu$ thick, after treatment with Lugol's solution, bodies were seen of a brown-black colour measuring from 5 or 6 to 20$\mu$ in diameter. The bodies generally had a round or oval form and often appeared to consist of a central more deeply stained part and of a peripheral lighter portion similar to a capsule. If, after treatment with Lugol's solution, the excess of this was removed with filter paper and substituted by some glycerol to which a small drop of sulphuric acid was added on the slide, the bodies became at first bluish and then deeply black. The authors were also able to see the same bodies in an unstained condition in specimens mounted in glycerol, as well as in preparations stained either by Giemsa's solution or Heidenhain's iron haematoxylin method. The authors are of the opinion that their 'bodies' are different from ordinary corpora amylacea, and are inclined to consider them almost as specific of lethargic encephalitis in the sense that 'they might be the expression of a reaction of the nervous tissue, accompanying and perhaps including the specific virus'. Gamma has seen the same bodies and agrees with Volpino and Desderi in regard to their tinctorial and microchemical characters, as well as to their frequent occurrence in the nervous tissue from cases of lethargic encephalitis. But he points out that they are not specific of this disease, and that very likely they are only a variety of the well-known amyloid bodies repeatedly described in the nervous tissue of aged subjects and in various pathological conditions. C. d. F.

**Sanfelice, F.** Delle mutazioni che presentano i bacilli acidoresistenti nel passaggio attraverso gli animali. [**Changes shown by acid-resisting bacilli on passing through the animal organism.**] *Ann. d'ig.*, 1920, **30**, 1.

On two different occasions the author was able to isolate from agar plates inoculated with material from cases of glanders an acid-fast bacillus of which he now gives a brief description. In ordinary preparations and in those stained by methods generally used for the demonstration of *B. diphtheriae* this non-motile and non-sporing bacillus appeared in the shape of elongated or ovoidal rods sometimes segmented, sometimes provided with bulbous extremities. True branching forms could be seen in some specimens. The bacillus, which morphologically resembled *B. diphtheriae*, was found to be Gram-positive and to occur, in specimens stained by the Ziehl-Gabbet method, as acid-fast and non-acid-fast forms, the latter being sometimes more numerous than the former. In agar plates the bacillus formed deep and superficial colonies. The deep colonies were small, well delimited, and of a coral red colour; the superficial ones were, as a rule, larger, some of them even reaching the size of a lentil; they were often umbilicated and of a pinkish colour, which in course of time also took on a coral red tone. When touched with a platinum needle the colonies were easily displaced *in toto*. The germ grew well at 20°–22° C. also in other media such as gelatin, bouillon, potato, milk; it did not fluidify the gelatin, and in bouillon culture gave origin to the formation of a superficial pellicle from the inferior surface of which small tuft-like particles could be seen detaching and falling to the bottom of the test-tube when this was gently shaken. Slant agar cultures were similar to those obtainable from human tuberculosis. All agar culture remained alive for months, viz. when the mediums had already become completely desiccated.

A suspension of the bacillus in physiological solution was made from an agar culture and injected intravenously into a rabbit. The animal died after 22 days, and the liver, lungs, meninges, and spleen were found beset with greyish-yellow nodules similar to miliary tubercles. From the nodules the same acid- and alcohol-fast bacilli described above were recovered, but their aspect was now extremely like that of true tubercle bacilli; the branching and club-shaped forms had disappeared; the colonies were less intensely coloured and did not grow so well at 20 or 22° C.; the number of the non-acid fast forms on the whole diminished. Also from a histological point of view the nodules could hardly be distinguished from true miliary tubercle.

By means of the acid-fast bacilli recovered from the first rabbit other animals were inoculated intravenously; amongst them a rat which died four months afterwards and had its lungs entirely beset with miliary nodules like those seen in the first rabbit. With the material obtained from this rat a guinea-pig was inoculated subcutaneously. The animal died after 22 days and showed lesions which could not be distinguished either histopathologically or bacteriologically from those caused by the inoculation of true tubercle bacilli in control animals. As a matter of fact all the non-acid-fast forms noted above had entirely disappeared, and the acid-resisting forms were now not only morphologically identical with true tubercle bacilli, but had lost the power of growing at 20 or 22° C., colonies of a greyish colour being obtainable only at 37° C. in sealed tubes of Petroff's medium.

C. d. F.

**Hall, I. C. Chemical criteria of anaerobiosis with special reference to methylene blue.** [**B**] *J. Bacteriol.*, 1921, **6**, 1.

In this paper the author reviews the value of methylene blue as an indicator of anaerobic conditions in the growth of bacteria. The decolorization occurs at a definite point in the extraction of oxygen, but this point is not necessarily the optimum for all anaerobes. An alkaline reaction is essential, but alkali alone is not sufficient. It is necessary to have present in addition, either glucose, peptone, or agar. The rapidity of the decolorization of methylene blue solutions depends upon the degree of alkalinity, reduction taking place without even heating if sufficient alkali is present. Recolorization in very slightly alkaline solutions need not imply oxygenation but may be due to acidification by $CO_2$ from the air. The bleaching action of animal and plant tissues is due to two factors. First to a reducing substance which may be extracted from the tissue, and second to mere adsorption of the stain. The futility of liquid oils for the exclusion of oxygen is commented upon and contrasted with the satisfactory behaviour of semi-solid or solid substances of the same type.

P. F.

**Gates, F. L., and Olitsky, P. K. Factors influencing anaerobiosis, with special reference to the use of fresh tissue.** *J. Exper. M.*, 1921, **33**, 51.

Methylene blue with either glucose or peptone in slightly alkaline solution is a good indicator of absence of oxygen. Liquid paraffin is useless as a seal for excluding oxygen, but paraffins remaining semi-solid at 37° C., e.g. solid vaseline, are satisfactory by virtue of their consistency. Hard paraffin may be less useful owing to expansion of the glass and rupture of the contact with the paraffin seal. The value of fresh tissue depends upon the amount used, and a larger fragment than usual is required to establish an adequate anaerobic zone. Serum and ascitic fluid, having no reducing properties, should be assisted by the addition of glucose or peptone. Semi-solid media without a seal prevent the return of oxygen to the depth of the tube if it is deep enough. McIntosh and Fildes's anaerobic jar is a further aid in establishing prompt anaerobic conditions, especially through the negative pressure brought about by the combustion of the oxygen with hydrogen and the consequent diminution in the tension of oxygen dissolved in the medium. P. F.

**Bieber, W.** Untersuchungen über die Schutzwirkung des Behringschen Diphtherieschutzmittels T. A. in der Praxis. [**The practical protective value of Behring's toxin-antitoxin mixture against diphtheria.**] *Deutsche med. Wchnschr.*, 1920, **46**, 1184.

In 1913 Hahn and Sommer carried out a series of inoculations of children in the Magdeburg district with toxin-antitoxin mixtures as a protection against diphtheria, and the present author has carried out an inquiry into the ultimate effect of this experiment. He found that 15 per cent. of 3,275 uninoculated children were attacked and 4·6 per cent. of 1,097 inoculated. A number of these latter were, however, only inoculated once (instead of twice) and only 3·3 per cent. of fully immunized children developed the disease. Thus the protection was not absolute, but nevertheless important. P. F.

**Gray, G. A., and Meyer, Bertha I. Diphtheria carriers and their treatment with mercurochrome.** *J. Infect. Dis.*, 1921, **28**, 323.

Mercurochrome (a 'bisodium salt of dibrom-oxymercury-fluorescine') was dropped into the noses and painted on the tonsils in 1·2 per cent. solution. 88 out of 90 men were freed from *B. diphtheriae* after an average of 19 applications in an average of 12 days. The criterion of cure was three consecutive negative cultures at two-day intervals, but while treatment was still applied. The third negative swab was taken 24 hours after the last treatment. No mention is made of subsequent cultures to check the results.
P. F.

**Simmons, J. S., Wearn, J. T., and Williams, O. B. Diphtheria infections with particular reference to carriers and to wound infections with *B. diphtheriae*.** *J. Infect. Dis.*, 1921, **28**, 327.

75 cases of diphtheria and 102 carriers were observed, 37 of the cases being in-patients or attendants of the hospital. The virulence of 52 strains for guinea-pigs was tested. Those obtained from wounds showing evidence of membrane were all virulent and nearly all from convalescent cases.

About half, however, of the strains obtained from contacts and apparently normal wounds were avirulent in doses of 1·5 c.c. of a 72-hour broth culture. The fermentation reactions of 32 strains were tested. All virulent strains except one fermented glucose and maltose but not saccharose. The exception was a saccharose fermenter from a wound. P. F.

**Doerr, R., Schnabel, A.,** und **Vöchting, K.** Das Verhalten der Körpertemperatur beim Fleckfieber des Menschen und der experimentell infizierbaren Laboratoriumstiere. [**The behaviour of the body temperature in typhus in man and in animals that can be experimentally infected.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **31**, 249.

This is an analysis of 46 temperature charts taken from human beings, monkeys, or guinea-pigs infected with the virus of typhus fever. There is a definite type of pyrexia peculiar to the disease, although departures from the type may be induced in different human beings according to age and race and in animals according to their varying powers of reacting to a pyrogenic irritamentum. There appear to be two forms of incubation, the one, short (less than 8 days), which results from the inoculation of guinea-pig passage virus, the other, long (10 to 12 days), which is seen in the natural communication of the disease or in the artificial inoculation of human beings or guinea-pigs with typhus blood or louse virus. Virulicidal serum prevents the pyrogenic effect of typhus virus in guinea-pigs. Typhus serum stops a typhus infection only if the serum is given shortly after the dose of virus. W. B.

**Kaneko, R.,** und **Morihana, S.** Untersuchungen über die Identität der *Spirochaeta icterohaemorrhagiae* (Inado und Ito) und der *Spirochaeta icterogenes* (Uhlenhuth und Fromme) und über das Verhalten der *Spirochaeta hebdomadis*, des Erregers des Siebentagefiebers ('Nanukayami'), gegenüber der *Spirochaeta icterogenes.* [**Researches on the identity of *Spirochaeta icterohaemorrhagiae* (Inado and Ito) and *Sp. icterogenes* (Uhlenhuth and Fromme) and the relation of *Sp. hebdomadis*, the cause of seven-day fever (Nanukayami), to *Sp. icterogenes.***] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **31**, 201.

This paper deals with the relationship of *Spirochaeta icterohaemorrhagiae* of Inado and Ito, and *Sp. icterogenes* of Uhlenhuth and Fromme. Morphologically the two cannot be differentiated, and while the Japanese race appears to be more virulent the immune reactions are so similar that the authors argue for the identity of the two. The examination of a third organism, *Sp. hebdomadis* (Ido, Ito, and Wani), which is the cause of a seven-day fever long known in Japan as 'Nanukayami', shows it to be similar in form to the other two spirochaetes, although in its immune reactions it behaves in a manner altogether different. W. B.

**Douglas, S. R. The question of serological races of *V. cholerae* and the relation of some other vibrios to this species.** *Brit. J. Exper. Pathol.*, 1921, **2**, 49.

All the strains of *V. cholerae* investigated belonged to one serological race, and as these strains came from widely different sources it is probable that there is only one serological race of *V. cholerae.* The advantage of using emulsions made by formolizing broth cultures, as recommended by

Dreyer, when comparing the agglutinating properties of a series of strains of the same organism is sharply brought out. After continued subculture on artificial media, emulsions of *V. paracholerae* A acquired the property of being agglutinated by cholera agglutinating sera, but these emulsions had no power of absorbing the agglutinins for emulsions of the homologous vibrio. This property was not lost either by repeated daily subculture in fluid media or by passage through a series of guinea-pigs sufficiently numerous completely to restore the virulence of the organism. Of the El Tor vibrios, the strains known as A, 4 and 5 behaved, both in their agglutinating and absorbing properties, as true *V. cholerae*, and should therefore be considered as belonging to this species. Strain 10 behaved in an exactly similar manner to *V. paracholerae* A, being agglutinated by an antiserum prepared from this organism and absorbing the specific agglutinins from the *V. paracholerae* A antiserum, and must therefore be considered as belonging to this species. *V. nasik*, *V. paracholerae* B, and the El Tor vibrio 35 had no serological relation with either *V. cholerae* or *V. paracholerae* A and could not be classified. P. F.

**VALLARDI, C.** (1). Rilievi epidemiologici e clinici sulle dissenterie da protozoi nella Campagna d'Oriente. [**Epidemiological and clinical notes on protozoan dysentery.**] *Atti d. Soc. lomb. di sc. med. e biol.*, 1920, **9**, 81.

**VALLARDI, C.** (2). Intorno alla sierodiagnosi nelle infezioni dissenteriche bacillari. [**On sero-diagnosis in bacillary dysenteric infections.**] *Atti d. Soc. lomb. di sc. med. e biol.*, 1920, **9**, 340.

**VALLARDI, C.** (3). Intorno alle forme dissenteriche miste amebico-bacillari. [**On mixed dysenteric forms.**] *Atti d. Soc. lomb. di sc. med. e biol.*, 1920, **9**, 419.

**VALLARDI, C.** (4). Studi intorno ad una epidemia di disenteria bacillare. [**Studies on an epidemic of bacillary dysentery.**] *Ann. d'ig.*, 1920, **30**, 544.

Little practical value can be attributed to agglutination for the identification of bacillary dysenteric forms, both because agglutinins generally appear many days after the beginning of the disease, when the germs have been already identified by means of cultures, and because agglutinins may be practically absent from the serum of typical cases of bacillary dysentery. If the serum-reaction is used because no other diagnostic means are available, agglutination should be attempted with various dysentery strains and with many samples of serum obtained at intervals of a few days, particularly when the first attempts have been attended by negative results. Agglutination has a greater importance when used for the diagnosis of dysenteric forms already in the convalescent stage; the reason for this is that specific agglutinins may persist for some months in the serum of dysenteric patients. These conclusions are based on a very large experience gained by the author in Macedonia during the years 1917–19. It is interesting to note that in many cases, besides the specific agglutinins, he also traced secondary ones reacting with germs belonging to the group of *B. typhosus* and *B. paratyphosus*. In 17 cases a mixed infection, viz. a primary combination of amoebic and bacillary dysentery, was observed. According to the author these dual dysenteric forms are perhaps more frequent than we at present think, particularly in subjects in a very wasted condition. C. d. F.

**Tibaldi, E.** Sopra una nuova specie di ameba parassita trovata nelle tonsille (*Entamoeba macrohyalina*). [**On a new species of parasitic amoeba occurring in the crypts of the tonsils (*Entamoeba macrohyalina*).**] *Ann. d'ig.*, 1920, **30**, 613.

Before describing the new species of parasitic amoeba discovered in the crypts of human tonsils, the author summarizes the history and characteristics of *Entamoeba gingivalis*, a full account of which has been recently given by C. Dobell in his monograph *The Amoebae living in Man*, published for the Medical Research Council by John Bale, Sons and Danielsson.

*Entamoeba macrohyalina* has a diameter varying between 24 and 40 $\mu$, and generally appears as a roundish, ovoidal, or elongated shape provided with short lobose pseudopodia. The well-developed ectoplasm is quite sharply differentiated from the endoplasm it surrounds because of its hyaline aspect. In fact this large ectoplasmic halo, which appears faintly and homogeneously coloured in preparations stained by Giemsa's fluid, forms one of the chief characteristics of the new species. The more readily stainable endoplasm has a spongy structure and aspect, sometimes thick and granular, sometimes thin and filled with a variable number of vacuoles. In the endoplasm ingested bacteria are often observed, as well as nuclear remains of more or less disrupted salivary corpuscles and leucocytes, as frequently happens in the case of *E. gingivalis*. In fresh living specimens a pulsating vesicle and rather sluggish movements can be seen, while little-developed and typically rounded pseudopodia are put forth. The nucleus of *E. macrohyalina* is roundish but not so typically spherical and vesicular as that of *E. gingivalis*. Its diameter, in stained specimens, varies from 3 to 6 $\mu$. The nuclear membrane is only slightly visible; the chromatin granules, always present in a considerable number, appear in the resting nucleus as small lumps which, without being so closely packed together as by *E. gingivalis* or *E. coli*, are massed one on the other so as to leave free a central area of triangular or polyhedrical form. In this irregularly shaped area a thin network may sometimes be detected, but not a distinct karyosome. *E. macrohyalina* appears to reproduce by division into two, and indeed Tibaldi figures and refers to various stages of a mitotic process, of which, however, he does not give a sufficiently clear description, influenced probably by the fact, already pointed out by Dobell, that also in the case of *E. gingivalis* division by mitosis has not as yet been properly described.

C. d. F.

**Dudgeon, L. S. Blackwater fever.** *J. Hyg.*, 1920, **19**, 208.

Dudgeon has followed his studies on malaria by a long paper on blackwater fever. His conclusions (somewhat abbreviated) are as follows: (1) True jaundice occurred in a high percentage of fatal cases. Haemoglobinaemia occurred in the acute stages. No auto-agglutination or autohaemolysis was discovered. Malaria was present in all cases. (2) The most important post-mortem findings were fatty degeneration of the myocardium, reduction in the lipoid content of the adrenals, enlargement of the Malpighian corpuscles of the spleen. In many cases there were haemorrhages and foci of necrosis in the liver, and haemorrhages into the kidneys. (3) Alcoholic and acetone extracts of the dried residue of the urine were highly haemolytic. The same results were obtained from the dried organs.

These results were not obtained from the organs of cases dying of malaria. (4) No evidence tending to incriminate quinine administration was met with. (5) Clumps of red cells were found in the urine in some cases. (6) Blackwater fever was most frequent during the months of March and April, when the temperature in Macedonia was at the commencement of its upward summer rise. No evidence was obtained that blackwater fever is in any way related to anaphylaxis.

The last sweeping statement is not apparently supported by any particular evidence, and Dudgeon has no alternative theory to account for the blood destruction. The conception of anaphylaxis has been so much enlarged in recent years that the mere statement that no signs of it are found needs to be supported by some account of what signs were looked for or would have been accepted as evidence of an anaphylactic factor in the disease.

G. W.

**LÉVY, P.-P.** L'interprétation des hémocultures. [**Interpretation of blood-cultures.**] *Presse méd.*, 1921, **29**, 296.

Lévy calls attention to the colour changes which occur respectively in sterile and positive haemo-cultures. The positive culture always shows a violet colour due to reduced haemoglobin, the negative a shade depending on the mixture of oxy- and met-haemoglobin and varying from bright red to brown. The colour is best appreciated in the film of corpuscles deposited from a culture in the incubator. Lévy has never found his 'réaction du virage globulaire' fail, and has several times caused to be re-examined cultures supposed to be sterile by his laboratory assistants. G. W.

**LUMIÈRE, A.**, et **CHEVROTIER, J.** Sur un procédé simple et inoffensif permettant d'éviter le choc anaphylactique. [**A simple and harmless method of preventing anaphylactic shock.**] *Compt. rend. Acad. d. sc.*, 1920, **171**, 741.

L. and C. recall the work of Besredka, Roux, and others, who showed that anaphylaxis could be prevented if the animal experimented on was under the influence of certain drugs like ether, chloral, &c. They find that if a 5 per cent. solution of sodium hyposulphite is substituted for the normal saline in the fluid containing the foreign protein, the *immediate* onset of anaphylactic shock can be absolutely prevented. Further work is being done on the question of the applicability of the method to therapeutic sera. L. and C. think that the method is capable of considerable practical use.

J. R. P.

**TALLO, F.** Azione *in vitro* del neosalvarsan sui bacilli del carbonchio da coltura (senza capsula) e sui bacilli provenienti dall' organismo animale (con capsula). [**Action *in vitro* of neo-salvarsan on *B. anthracis* from cultures (without capsule) and from the animal organism (with capsule).**] *Riforma med.*, 1920, **36**, 1145.

Neo-salvarsan diluted with bouillon has *in vitro* a strong bactericidal action on *B. anthracis* from cultures. This action is very little altered by the substitution of the bouillon with blood-serum in the mixture of bacilli and drug. But in the same experimental conditions neo-salvarsan appears to have no action on *B. anthracis* from the animal organism, viz. when provided with a capsule. C. d. F.

**Piccininni, F.** (1). Osservazioni epidemiologiche ed anatomo-patologiche sulla peste nei ratti. Ricerche sperimentali sulla immunità dei ratti contro la peste. [**Epidemiological and anatomo-pathological observations on rat plague. Experimental investigations on the immunity of rats against plague.**] *Ann. d'ig.*, 1920, **30**, 484.

**Piccininni, F.** (2). I veicoli d'importazione del contagio della peste in Italia e i mezzi di difesa. [**Means of importation of plague into Italy and preventive measures.**] *Ann. d'ig.*, 1920, **30**, 604.

The author having had, as director of the bacteriological laboratory of the port of Naples, the opportunity of closely studying the various epizootics of rat plague which have occurred in that port during the last few years and in that of Castellamare di Stabia in 1919, gives in his first paper an account of his observations and experiments. These led him to conclusions which in many points agree with the results attained by other investigators in different countries and may be summarized as follows:

The simple post-mortem examination of suspected rats is not sufficient to exclude plague infection because gross morbid changes, and even the enlargement of lymph glands, are often misleading when present, and may sometimes be completely absent. Enlargement and congestion of the spleen are an almost constant feature of plague-infected rats, but they also are not pathognomonic of pest. Microscopic and cultural examination as well as animal experiments are therefore necessary both for the diagnosis and for the exclusion of rat plague, and these should be carried out even when gross morbid changes are completely absent. Also the microscopic and cultural examination, upon which one can entirely rely in the case of animals infected experimentally, present a number of fallacies in the case of rats delivered dead at the laboratory. Plague bacilli may be present in a very small number either in the blood or in the internal organs such as the spleen and liver; sometimes they are less numerous in blood films than in spleen smears, but in some cases the reverse holds good, and in the liver they may be extremely rare. Putrefactive micro-organisms are almost always found in the blood and internal organs of rats dead of plague, and such bacteria may present forms resembling very closely plague bacilli, or be so numerous as to render cultural examination extremely difficult and, at any rate, not reliable for diagnostic purposes. For inoculation experiments guinea-pigs should be preferred, because they show anatomo-pathological lesions so typical of plague as to render further investigations unnecessary. If guinea-pigs are not available mice (*Mus musculus*) should be used, avoiding as far as possible having resort to rats. In this connexion it should be noted that the author was not provided with white rats and used for his experiments ordinary rats (*Mus decumanus* and *Mus rattus*) which, he points out, may be spontaneously immune against plague or may, in some cases, become infected and die of pest, the post-mortem and microscopic examination being nevertheless attended by dubious or even negative results.

At the end of his account, but chiefly in his second communication, the author deals with the measures to be taken in order to protect the population of coast towns from the possible danger of plague epidemics. As far as Italy is concerned the only means of importation of plague to be feared are, in his opinion, represented by infected rats, which may reach Italian ports on ships arriving from every part of the world. The danger of direct transmission from man to man is almost negligible in the case of Italy because, with the exception of some endemic plague foci in Cyrenaica, all others, from which infected individuals might reach Italian ports, are situated at a distance of more than five days by sea, this time being sufficient for cases of plague to have passed the incubation period and to be easily recognizable before landing. Also the possible transmission of plague from infected rats to man by fleas has, according to the author, little importance in the case of civilized countries. The same can be said of the possible transmission of plague by means of merchandise because, with the exception of relatively rare instances in which infected dead rats were found or delivered with it, the possibility that it might convey the disease because of having been handled by infected people is practically much reduced by the fact that the *B. pestis* is killed or much attenuated in its virulence by exposure to air, sunlight, &c. Preventive measures should, therefore, be concentrated in the untiring bacteriological investigation of all suspicious rats caught alive or found dead on board ships, in storage places, warehouses, dockyards, and generally in the neighbourhood of ports, as well as in the systematic destruction of rats by all available means. This, however, is not considered sufficient by the author, who emphasizes the necessity of completely separating the sewerage of coast towns from that of their ports. As ascertained by other authors, and confirmed by Piccininni's experiments, a certain time after the outbreak of a plague epizootic, rats become spontaneously immune against it, and they may thus be said to help in preventing the spreading and continuation of the disease among themselves. But if, particularly at the beginning of a fresh epidemic, non-immune rats can penetrate into the town sewerage, the danger that they may transmit the infection to the rats existing there, and through them to the human population, becomes very great. To prevent it no measure will ever be so efficacious as the complete separation of town and port sewerage. As an example, the author points to the town of Naples, where such a condition existed until quite recently, and where, in spite of various outbreaks of rat plague, no case of the disease was recorded among the inhabitants of the town. C. d. F.

**IRALA, J.** Ricerche sulla fagocitosi. [**Investigations on phagocytosis.**] *Ann. d'ig.*, 1920, **30**, 28.

Emulsions of *Staphylococcus pyogenes aureus* were used by the author for various experiments which led him to the following conclusions: (1) Ultra-violet rays increase at first the phagocytic power of human leucocytes, but this action rapidly diminishes because prolonged exposures (ten to twenty minutes) of leucocytes to ultra-violet rays noticeably alter them. As, however, Ciancio (*Riforma med.*, 1919, **35**, 596) has recently shown that *Staphylococcus pyogenes*, after exposure to the same rays, becomes more easily the prey of leucocytes, it remains undecided whether the beneficial action of ultra-violet rays and sunlight in certain affections of the skin is due either to a diminished resistance of the germs or to an increased phagocytic power of the leucocytes or to both factors. (2) Calcium chloride prevents phagocytosis if bacteria are alive, but increases it if they are dead. This may explain why certain bacteria (e.g. *B. tetani*) are innocuous for certain animals when inoculated alone, but are fatal if a small quantity of calcium chloride is added to the emulsion used for the inoculation. (3) Lactic acid, in concentrations of 0·5 to 0·05 per cent., diminishes the phagocytic power of leucocytes. And as the content in lactic acid is noticeably increased in the human blood of fatigued subjects, Irala's results show that lactic acid probably plays a rôle in the diminished resistance to infection of over-tired organisms. C. d. F.

**Alexander, W. An inquiry into the distribution of the blood groups in patients suffering from 'malignant disease'.** *Brit. J. Exper. Pathol.*, 1921, **2**, 66.

The blood-group of 50 cases of malignant disease was determined, and the incidence of each compared with that in 125 cases of other diseases and 50 normal persons. It was found that, while persons belonging to all four groups were liable to malignant disease, those in Groups I and III appeared to be peculiarly susceptible and the clinical type of disease was, generally speaking, more malignant. P.-F.

**Weinberg, M.**, et **Kepinow, L.** Des leuco-agglutinines. [**Leuco-agglutinins.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 380.

Weinberg and Kepinow have studied the agglutinating properties of certain substances, mostly bacterial toxins, on leucocytes, as follows: 5 c.cm. of a sterile 10 per cent. emulsion of Mellin's food are injected intraperitoneally into a guinea-pig, which has previously received 1 c.cm. of the same emulsion (length of time between the two injections not stated). The animal is bled completely 14–16 hours after the second injection. Some 30–40 c.cm. of 1 per cent. sodium oxalate in water are introduced into the peritoneal cavity. The peritoneal exudate, which usually contains 80–100 thousand leucocytes per c.mm., is preserved in the ice-chest and keeps quite well for 2 to 3 days. 0·3 to 0·5 c.cm. of the suspension of leucocytes and a sufficient quantity of normal saline to make up 2 c.cm. in all are placed into a series of test-tubes, and after adding gradually diminishing quantities of the toxin, starting from 0·3 c.cm., the tubes are incubated at 37° C. for 2–3 hours, when the results are read after carefully turning each tube upside down. Obvious flocculi caused by the agglutination of the leucocytes will be noticed. Auto-agglutination of the leucocytes is never so pronounced as to cause any difficulty in reading the results. Weinberg and Kepinow studied the toxins of *B. perfringens*, *Vibrion septique*, *B. sporogenes*, *B. tetani*, *B. diphtheriae*, *B. influenzae*, staphylococci, pneumococci, and a few others, and draw the following conclusions:

(1) Bacterial leuco-agglutinin is destroyed by exposure to 58–60 C. for ½ hour in a water-bath.

(2) The leuco-agglutinating power of a bacterium varies in direct ratio with its virulence, but not with its toxicity in comparison with another bacterium, e. g.: *Pneumococcus*, *B. diphtheriae*, and *Vibrion septique* are extremely active, but *B. sporogenes* and *B. histolyticus* quite inactive, and a non-pathogenic pneumococcus was also inactive. The same experiments can be performed *in vivo* and give the same results. Horse serum agglutinates washed guinea-pig leucocytes. The leucocytes of a guinea-pig in a state of anaphylaxis are more auto-agglutinable than those of a normal one. In the case of *Vibrion septique* the peritoneal exudate is poor in leucocytes, which tend to congregate in the terminal portions of the mesenteric lymphatics. J. R. P.

**Nicolle, C.**, et **Cuénod, A.** Nouvelles acquisitions dans l'étude expérimentale du trachome. [**Further additions to our knowledge of experimental trachoma.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 1011.

N. and C. sum up the results of their work on the experimental study of trachoma as follows:

(1) Experimental trachoma in *Macacus innuus* may last 15–18 months and more, is subject to relapses, and may provoke a keratitis.

(2) The virus of trachoma causes in the rabbit granulations, which may last a year and which are still virulent for *M. innuus* after that time.

(3) The virus of trachoma lives at least 37 days in the testicle of the rabbit.

(4) A first attack in the rabbit or in *M. innuus* does not protect against a second artificial infection. J. R. P.

**Karsner, H. T.**, and **Swanbeck, C. E. The removal of particulate matter from the pleura.** *J. Med. Research*, 1920, **42**, 91.

This work consisted in injecting suspensions of carmine or lamp-black into pleural cavities of 20 cats and studying the position of the pigments at different periods. The pigment was taken up by the pleural endothelial cells *in situ* and was carried by the migration of these cells into the lymph nodes of the pulmonary hilum and of the mediastinum. Occasionally a pleural endothelial cell full of pigment could be seen leaving the surface to reach an underlying lymphatic, and similar cells were found in and round the lymphatics. No cellular inflammatory exudation and but little fibrin was found in the pleural sac. All the carriage of the pigment was done by phagocytosis by the pleural endothelium. No extracellular pigment was seen in the tissues. The cells, full of pigment, travelled to the mediastinum from the parietal pleura and to the hilar lymph nodes via subpleural and peribronchial lymphatics from the visceral pleura. The parietal pleura appeared more active in the phagocytosis. Slight carbon pigmentation found in mediastinum or hilar lymph nodes of cats that were injected with lamp-black after death and artificially respirated is the evidence in support of the conclusion that 'the phagocytic power of the cells is a primitive function existing after the death of the animal'.

W. W. W.

**Permar, H. H. An experimental study of the mononuclear phagocytes of the lung.** *J. Med. Research*, 1920, **42**, 9.

Briscoe (1908) thought that the alveolar epithelial cell was the chief phagocyte of the lung for all foreign matter. Haythorn (1913) decided against the lining cell of the alveolus and pointed out that the alveolar phagocyte was a wandering cell, probably arising in vascular endothelium. Sewell (1918), ignoring the migratory activity of these phagocytes, which is not a characteristic of epithelial cells as a class, reverted to the view of Briscoe and was supported by Mavrogordato (1918).

In the present work, using rabbits and guinea-pigs, isamine blue was injected intravenously as a vital stain instead of Indian ink, to avoid confusion with the naturally occurring carbon dust in pulmonary phagocytes. It was given daily for from 8 to 11 days. As foreign material to produce phagocytosis heavy and light suspensions of carmine powder, or occasionally lithium carmine, were given intratracheally at periods varying from a few hours to 5 days before death. It was considered an important measure to continue the vital stain frequently after the intratracheal injection as the phagocytes seem to take up the isamine blue during the process of their production.

Examination was made chiefly by frozen sections and smears. Isamine blue was seen in swollen endothelium of pulmonary capillaries. All phagocytes were of mononuclear type, but varied in size from that of a polymorphonuclear leucocyte to 8 times that size. They were identical with the ordinary dust phagocytes and took the same paths. They were found at work in 1½ hours. They were found vitally stained and containing carmine, and sometimes also dust, in the alveoli and flattened out on the surface of the alveolar epithelium and insinuated between alveolar epithelial cells, and in the interalveolar septa. After five hours a few had reached the larger lymphatics and small intrapulmonary nodes. After 24 hours they were in the sinuses of the peribronchial glands. Numerous mononuclear cells heavily loaded with carmine, but without distinguishable vital staining, were also found in all these positions. The alveolar epithelium never contained carmine granules. Carmine pigment was only found in cells, never free in the tissue, but phagocytes might disintegrate after the period covered by these experiments. Clumps of mononuclear cells were constantly seen in the angles of the alveolar spaces and Permar regards these as phagocytes disposed here to be near the exit into the smallest lymphatics, which, according to Miller, originate in the walls of the atria or ductuli alveolares. He rejects Sewell's view that these clumps are a specialized form of alveolar epithelium. Control animals, vitally stained but without intratracheal stimulation of phagocytosis, showed little vital stain in the lungs. This confirms the results of many previous investigators The vital stain was only found in the lung in a few capillary endothelial cells. In the controls, neither pulmonary epithelium nor the endothelium of lymphatic channels took the isamine blue, though the sinus cells of the peribronchial lymph nodes sometimes did and sometimes did not.

Proliferation of endothelium of small pulmonary capillaries was therefore considered to provide all the phagocytes. Occasionally proliferation occurred in the endothelium of larger branches of the pulmonary arteries. Amoebic movement must have carried the phagocytes along some part of their route; at other parts the lymph-stream would assist. In one surprising experiment vitally stained cells were completely absent from the lungs of a rabbit three days after intratracheal carmine, though carmine phagocytes were present. Only a few polymorphonuclear leucocytes appeared in the pulmonary tissues and alveoli. They were stained with isamine blue but never acted as phagocytes of carmine. Blood films showed no vital staining in the circulating mononuclear leucocytes.

W. W. W.

**DUCCESCHI, V.** Azione dell' alcohol etilico sull' organismo. [**Influence of ethyl alcohol on the organism.**] *Ann. d'ig.*, 1920, **30**, 91.

The increased consumption of alcoholic beverages observed in Italy during the last few years has induced the author to summarize in the present communication the results of his histochemical investigations on the effect of alcohol on animal and human organisms, published in the

*Arch. di Fisiol.* between 1915 and 1918. These studies are important both because our knowledge on the subject is of an almost exclusive morphological character, and because new light is thrown on the still obscure problem of the influence of alcohol, particularly when consumed in small quantities for very long periods. Ducceschi's investigations deal chiefly with the content in cholesterol, lecithin, and neutral fat in the blood of human beings used to taking alcoholic drinks, as well as in the blood and various organs of dogs kept under the influence of alcohol. The following are the principal conclusions reached by the author: Alcoholic intoxication causes a remarkable increase in the content of cholesterol and fatty acids in the circulating blood. The phosphatides (lecithin) are also increased, but in a lesser degree and not constantly. These results show that the daily and prolonged consumption of relatively large quantities of alcohol produces a constant increase of the total fat in the blood, or, in Ducceschi's words, a 'lipoidolysis', this being probably of cellular origin. As to the organs of experimentally intoxicated animals, the most affected appears to be the liver, the total fat of which may be 300 per cent. above the normal average, and is generally accompanied by an increase in the amount of cholesterol, though in smaller proportions. Also the dry residue of the liver is greater in intoxicated dogs than in normal ones. The suprarenal glands of intoxicated dogs show a constant diminution (about 40 per cent.) of the cholesterol with a slight increase of the total fat and dry residue. Constant and characteristic alterations of the lipoid content were not, as a rule, observed in the kidney and testis of the same animals; but the total fat and cholesterol of the kidney were found to have increased in two dogs intoxicated with alcohol when fasting. Hence the conclusion that inanition favours the alteration of the lipolytic indexes. C. d. F.

**Torraca, T.** Per la conoscenza dell' epitelioma adenoide cistico (Brooke) o trico-epitelioma papuloso multiplo (Jarisch). [**On *epithelioma adenoides cysticum* (Brooke) or *tricho-epithelioma papillosum multiplex* (Jarisch).**] *Riforma med.*, 1920, **36**, 974.

This malady has also been described as adenoma of the sweat glands (Perry), acanthoma adenoides cysticum (Unna), multiple benign cystic epithelioma (Stelwagon), hydradenomes eruptifs (Jaquier and Darier), syringocystoma, syringoma, &c. It is characterized by usually small, tubercular, or nodular tumours of a pinkish, pearly, or pale-yellowish colour, generally situated on the face, the upper part of the trunk, and less frequently the arms. In size they generally vary from a pin-head to a pea, projecting above the surface, and have a shining semitranslucent appearance. Histologically they consist of irregularly rounded, oval, and elongated masses and tracts of epithelial cells similar to those of the basal layer of the epidermis and external root-sheath of the hair-follicles. These masses are sometimes distinct, sometimes composed of intercommunicating bands and tracts, in some places resembling coil-ducts; cell-nests are occasionally seen as in malignant epithelioma. Lying in the tracts, or more generally in the masses, cysts can be observed, circular or oval in shape, filled with either purely colloid matter or partly with colloid and partly with concentric layers of apparently horned epithelium. The points of resemblance with and difference from rodent ulcer have recently been particularly dwelt on in this country by H. G. Adamson and Graham Little. The special features of the case observed by Torraca were the great number of tumours on the skin of the trunk, face, and head, and the quite uncommon size of some of them, which were 'as large as half an orange'. Torraca thinks that the lesion is clinically and pathologically different from rodent ulcer and that its origin is to be attributed to an abnormal proliferation of the cells of the hair-follicles and sebaceous glands, this being due to a cause capable of acting at the same time on many distant points, such as perhaps one of the so-called morphogenetic hormones. C. d. F.

**Pannett, C. A., and Wilson, C. M. The influence of bile-salts on gastric function.** *Brit. J. Exper. Pathol.*, 1921, 2, 70.

It is shown experimentally in cats and man that the addition of a small quantity of sodium taurocholate to a test-meal is followed by an abnormally rapid evacuation of the stomach contents. P. F.

**Paton, D. Noel, and Watson, A. The aetiology of rickets: an experimental investigation.** *Brit. J. Exper. Pathol.*, 1921, **2**, 75.

(1) In young dogs under ordinary laboratory conditions a liberal allowance of milk-fat, up to even 14 gm. per kilo. of body-weight, does not prevent the onset of rickets. (2) Pups kept largely in the open air may escape the development of rickets on an intake of less than 1 gm. of milk-fat per kilo. of body-weight. (3) With scrupulous care as to cleanliness it is, at least sometimes, possible to rear pups free of rickets in the laboratory on an intake of only about 0·5 gm. of milk-fat per kilo. of body-weight, along with bread, provided that the diet affords an adequate supply of energy. (4) The energy value of the diet, however supplied, quite apart from the presence of any hypothetical antirachitic factor in milk-fat, would seem to play a part in controlling the development of rickets; but that it is only a contributory part is shown by the development of rickets in pups with a high energy intake if confined in the laboratory without scrupulous care as to cleanliness. (5) Milk-fat may be reduced to about 0·3 gm. per kilo. of body-weight, if its place is taken by an equal amount of lard, without the onset of rickets. (6) The results of these observations give no support to the conclusion of the Accessory Food Factors Committee of the Medical Research Council that rickets is a deficiency disease due to a lack of an antirachitic factor in the diet. P. F.

**Browning, C. H., and Gulbransen, R. The antiseptic potency of acriflavine, with considerations on the variability of results in testing antiseptics.** *Brit. J. Exper. Pathol.*, 1921, 2, 95.

Acriflavine in heated ox serum will sterilize *B. coli* in 1 in 100,000 and *Staphylococcus aureus* in 1 in 200,000. The action in peptone water is more pronounced in a slightly alkaline medium than in one more acid. The sterilizing concentration is independent of the size of the inoculum. Different specimens of acriflavine give similar results, but some are more irritating (therapeutic importance). No rapid exhaustion or deterioration of the antiseptic was found to occur in the medium. The occurrence of variation in the sterilizing dose in successive tests, and of irregularities, is noted, and their significance discussed. P. F.

**Bennett, T. I., and Dodds, E. C. The gastric and respiratory response to meals.** *Brit. J. Exper. Pathol.*, 1921, **2**, 58.

(1) Studied by means of gastric analysis and by estimation of alveolar $CO_2$ tension, normal men are found to fall into four distinct classes. (2) The results obtained by the two methods are found to confirm one another. (3) Cases showing achlorhydria during gastric analysis show a curve of alveolar $CO_2$ tension similar to that obtained in patients following gastrectomy. (4) Such cases show a fall in alveolar $CO_2$ tension at a later period, indicating normal secretion during the later processes in digestion. (5) Cases of hyperchlorhydria in healthy men have sometimes been found to show changes in alveolar $CO_2$ tension following meals which exceed what have previously been considered physiological limits. (6) Some normal cases occur in whom the processes of upper alimentary digestion are so rapid as to be only demonstrable by observations taken at very short intervals. (7) Cases which yield a high gastric acidity during digestion are usually found to show a relatively high tension of alveolar $CO_2$ even during the 'resting' phases of the stomach; in cases of achlorhydria the reverse is seen.
P. F.

**Cramer, W., and Mottram, J. C. Similarity of effects produced by absence of vitamines and by exposure to X-rays and radium.** *Lancet*, 1921, i, 963–4.

Cramer and Mottram compare the effects produced by absence of vitamines from the diet and by application of X-rays and radium. They find that vitamines are not essential to the life of the individual cell with the exception of the cells of the lymphoid tissues. All the lymphoid tissues examined—spleen, thymus, &c.—were tremendously atrophied. This was reflected in the blood-stream by a diminution of lymphocytes, but total numbers are not given. The differential figures show a relative increase of polymorphs. The authors claim that these changes are 'practically identical' with those brought about by X-rays and radium. There is, however, the very significant difference that with these latter agents the polymorphs are first diminished, and even when the total number of lymphocytes falls below normal they still show a high relative percentage. This is in sharp contrast to the figures given in this paper as the result of avitaminosis.
G. W.

**Loeper, M., Forestier, J., et Tonnet, J.** L'hyperalbuminose paradoxale du sang des cancéreux. [**Paradoxical hyperalbuminosis in the blood of cancer subjects.**] *Presse méd.*, 1921, **29**, 333–4.

Loeper and his co-workers studied the substances in the blood of those afflicted with cancer with particular regard to (1) proteins, (2) the ferments which break them up, and (3) the products of their destruction. In ordinary cases the proportion of blood albumins seldom exceeds 7·5 per cent. This figure may be lowered by hydraemia, cachexia, and malnutrition, or raised by the concentration associated with thirst, excessive vomiting, or polyuria. It is obvious that cancer is commonly associated with cachexia, &c., so that we should expect a low figure, but the authors find on the contrary a tendency in the opposite direction, and it is to the finding of an increased percentage (up to 11·0 per cent.) that they give the name 'hyperalbuminose paradoxale'. The degree of increase they find to depend on the size of the tumour present, and further that the albumin is predominantly globuline and derived from the tumour itself. These tumour proteins vary in composition, but it may be said that as a rule they are in no way toxic or injurious. They may give rise to albuminuria.

It is natural to expect that the body would provide some ferment capable of dealing with this excess waste of albumose, and the authors find in fact a great increase of an erepsin-like ferment. The activities of this ferment are attested by very high figures for total nitrogen in the serum.

It is true that but little of this work is new and some of it has been explored and in part at least abandoned for years past, but there is no doubt, as the authors point out, that along these lines it is not at all impossible that we should discover a practical clinical test for cancer. G. W.

**ALEZAIS** et **PEYRON**. Sur le mode de développement des tumeurs dites mixtes et des cylindromes de la région de la face. [**The development of so-called mixed tumours and cylindromata of the facial region.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 781.

A further contribution to the authors' previous work on the development of connected tissue from epithelium. In this case 60 tumours of the facial region, mostly mixed tumours of the salivary glands, are the subject of study. A minute description is given of the development of true collagenous fibres from the exoplasm of the epithelial masses.

J. R. P.

**BLOOMFIELD, A. L. The mechanism of the bacillus carrier state with special reference to the Friedlaender bacillus.** *Am. Rev. Tuberc.*, 1921, **4**, 847–55.

In a study of the conditions under which the Friedlaender bacillus lives in the carrier state, Bloomfield maintains that this and other organisms live and multiply in a focus of diseased tissue in the upper air passages, whence they are discharged to the neighbouring surfaces. Among 85 unselected individuals, he found 5·8 per cent., to be carriers of *B. Friedlaender*, and while this carrier state persisted throughout the period of observation, contacts showed no tendency also to become carriers. Attempts to produce artificially a carrier state by swabbing the tongue of a person with a freshly isolated strain of *B. Friedlaender* always proved futile; within 24 hours of the last inoculation this person was free from *B. Friedlaender*. This was the expected result, and it supported the view that a focus of infection is responsible for the carrier state. Differential cultures showed the breeding-place of the *B. Friedlaender* to be in the tonsil. Apparently these organisms do not become adapted to growth on the free surface of the mucous membranes. C. L.

## BIOCHEMISTRY

**Hart, E. B., Steenbock, H.,** and **Ellis, N. R. Antiscorbutic potency of milk powders.** *J. Biol. Chem.*, 1921, **46**, 309.

The authors draw attention to three main ways of preparing milk powders. Firstly there is the Merrell Soule or spray process. Secondly there is a spray process in which the milk is not condensed before being dried. In this the powder is cooled and removed within a few seconds of being dried. There is lastly the Just process. In this latter case the milk is dried on heated rolls. Hess and Unger found that milk dried by the Just process prevented scurvy successfully. The authors have confirmed these results. They find that the spray process of manufacture is more injurious to the antiscorbutic vitamine than the Just process. They, however, recommend the addition of some potent antiscorbutic source in the case of feeding with all milk powders, and draw attention to the variation that may be produced in the amount of vitamine in a cow's milk according to the feeding which the cow is receiving. R. A. P.

**Hawk, P. B., Smith, C. A.,** and **Bergeim, O. The vitamine content of honey.** *Am. J. Physiol.*, 1921, **55**, 339.

Strained honey contains only minimal amounts of the water-soluble B and the fat-soluble A vitamines. Comb honey contains moderate amounts of the fat-soluble vitamine. Honey does not contain the antirachitic vitamine.

W. C.

**Johns, C. O.,** and **Finks, A. J. Studies in nutrition. V. The nutritive value of soy bean flour as a supplement to wheat flour.** *Am. J. Physiol.*, 1921, **55**, 455.

Bread made with a mixture of 25 parts of soy bean flour and 75 parts of wheat contained a protein mixture and water-soluble vitamines adequate for normal growth. A similar bread containing 15 parts of soy bean flour and 85 parts of wheat flour likewise furnished adequate proteins and water-soluble vitamines for normal growth. These mixtures of the soy bean and wheat proteins were found two or three times more efficient than the proteins from wheat alone. W. C.

**van Anrep, G.,** and **Drummond, J. C. Note on the supposed identity of the water-soluble vitamine B and secretin.** *J. Physiol.*, 1921, **54**, 349.

In criticism of a paper by Voegtlin and Myers suggesting that secretin and the antineuritic vitamine are possibly identical. The authors find that highly active yeast extracts have no specific action on pancreatic secretion, and also that secretin can be extracted from the intestinal mucosa of cats which show the polyneuritic condition in a very marked degree.

O. L. V. de W.

**Hawk, P. B., Smith, C. H.,** and **Bergeim, O. The nutritive value of yeast in bread.** 1921, **56**, 33.

The addition of 5 per cent. yeast powder to flour makes a palatable bread with a greatly increased content in the water-soluble B vitamine Such bread is much more nutritious than ordinary bread. W. C.

**Stearns, G., and Lewis, H. B. Diet and sex as factors in the creatinuria of man.** *Am. J. Physiol.*, 1921, **56**, 60.

The observations confirm those of Krause that creatin occurs at intervals in the urine of normal women. There appears to be no direct relation between the creatin excretion and the phases of the menstrual cycle, as Krause supposed. Nor can it be explained as the result of a high protein diet. No explanation is given by the authors. It appears to the writer that it is less important to find an explanation than to recognize the fact that the appearance of creatin in the urine does not have the significance as an indication of abnormal metabolism which has been attributed to it.

W. C.

**Henderson, L. J. Blood as a physico-chemical system.** *J. Biol. Chem.*, 1921, **46**, 411.

It has been found possible to represent the ralations between the main varying factors in the blood upon one graph. The main variables taken are the free and combined oxygen of the whole blood, the free and combined carbonic acid of the serum, the hydrogen-ion concentration of the serum, expressed as $P_H$, and the chloride concentration of the serum. By choosing these variables there is a certain degree of simplification of the facts. However, some interesting things appear. The relations between these variables in the blood are arranged in equilibrium in such a way that the fixing of two of the variables determines the position of the remaining four. The chart expressing these relations, known as a nomogram, can be used for the prediction of possible conditions. R. A. P.

**Iversen, P.** Untersuchungen über die Verteilung der Phosphate zwischen Blutkörperchen und Plasma innerhalb und ausserhalb des Organismus. [**Experiments upon the distribution of phosphates between blood corpuscles and plasma *in vivo* and *in vitro*.**] *Biochem. Ztschr.*, 1921, **114**, 297.

The experiments are concerned with the partition of added phosphate between corpuscles and plasma in rabbits' blood. If a solution of $Na_2HPO_4$ is added to defibrinated rabbits' blood *in vitro*, there is a passage of a comparatively small amount of the added phosphate into the corpuscles within the first two hours. The main amount, however, remains in the plasma. If, however, a solution of the phosphate is injected into the living rabbit from which the kidney has been removed, the phosphate becomes gradually distributed in such a way that the main part comes into the corpuscles. The opinion is given that the phosphate in the living animal is stored in some combined form in which it is not ionized. Thereby more can pass into the corpuscle. The result seems of interest in connexion with the question of the equilibrium of ions between the corpuscles and the plasma. R. A. P.

**Davis, L. H., and Ellison, L. R. The source of diastases in the blood.** *Am. J. Physiol.*, 1921, **56**, 22.

The conclusion is reached that the pancreas is practically the only source of the diastases in the blood. W. C.

**Meek, W. J.**, and **Eyster, J. A. E. Reactions to haemorrhage.** *Am. J. Physiol.*, 1921, **56**, 1.

The effect of haemorrhage on the diastolic heart size of the dog has been studied by means of X-rays. In the intact animal haemorrhage amounting to about 2·1 per cent. of the body-weight is necessary before the diastolic heart size and the output are reduced. In the anaesthetized animal with open chest this occurs sooner, namely, when the total haemorrhage equals about 1·2 per cent. of the body-weight.

The explanation for the maintainance of cardiac output is that there is a constriction of venules and capillaries. In the intact animal the venules and capillaries of the ear may be seen markedly to constrict when the haemorrhage reaches about 2 per cent. W. C.

**Langfeldt, G. Blood-sugar regulation and the origin of the hyperglycaemias. 1. Glycogen formation and glycogenolysis. 2. Conditions of action of liver diastases. 3. Theory.** *J. Biol. Chem.*, 1921, **46**, 381.

Starting with an historical account of certain aspects of the question of sugar regulation, the author leads up to a theory of sugar metabolism.

In his classical researches upon the blood-sugar, Claude Bernard came to the conclusion that the blood-sugar was secreted by the liver. Sugar regulation was supposed by him to be controlled by reflexes received nervously from the medulla oblongata. Diabetes to him was therefore a nervous disease. Sugar was normally supplied to the organs as they needed it. Von Noorden made a change in this view by suggesting that the transformation of glycogen to sugar took place upon the passage of a chemical stimulus from the muscles to the liver.

The existence of the diastatic ferment in the liver cells *in vivo* has made it difficult to understand how the action of the ferment is prevented in the cell. Diastase and glycogen exist apparently side by side in the cell and yet there is not immediate hydrolysis to glucose. To account for this it has been suggested by Bang that pure liver diastase is inactive. The activator is sodium chloride, not ordinarily existent in the cell. By the secretion of the bile, the liver cell becomes permeable to sodium chloride. Adrenalin is also supposed to act in a somewhat similar way. Grode and Lesser, however, believe that diastase and glycogen exist separately in the cell and are brought in contact by certain substances such as adrenalin. The author considers all these views inadequate as they do not take into account the two processes of glycogen formation and glycogen breakdown. An examination of the literature leads him to conclude that the pancreas is really necessary for glycogen formation. In some experiments conducted by him, it was shown that a temporary increase in the amount of sugar in the blood produced by feeding with sugar disappeared quickly under normal circumstances. In depancreatized dogs it did not disappear nearly so quickly. This has led him to believe that the formation of glycogen depends upon the presence of the pancreas hormone. In further experiments he found that an increase of hydrogen-ion concentration in the portal vein in dogs led to a heavy glycogenolysis. He was therefore led to investigate the effect of reaction upon the action of liver diastase.

It was found that the optimum action of liver diastase differed under different conditions. In the presence of phosphate the optimum reaction (hydrogen-ion concentration) was at a more acid point than in the presence of added chloride. In both cases the optimum effect was at a more acid point than the blood reaction. Adrenalin addition had the effect of shifting the optimum to the alkaline side. The addition of thyroidin alone had no effect upon the hydrolysis. Simultaneous additions of thyroidin and adrenalin had a very strong effect. Pituitary extract had none.

Using these experimental facts the author builds up a theory of sugar regulation dependent upon the local conditions in the liver cell. Normally the liver diastase is acting in a medium too alkaline for its maximum effect. Under constant conditions of blood-flow and temperature in the liver, there is a constant supply of glucose to the blood. Part of this is used by the body, part is stored in the muscles, and the remainder is returned to the liver, where the pancreas hormone takes part in the re-formation to glycogen.

This theory can be extended to the hyperglycaemias. Hyperglycaemia may arise in one of three ways.

(1) By a change in the hydrogen-ion concentration of the liver so that the $P_H$ is identical with or close to the optimum of the action of diastase in the presence of salts.

(2) By a displacement of the curve of action of the diastase, by adrenalin for example, so that the optimum is close to the hydrogen-ion concentration of the tissue.

(3) By a deficiency of the pancreas hormone, which will give rise to a decreased formation of glycogen, and so to an excess of sugar in the blood.

(1) will be generally illustrated by the effect of acids upon sugar in the blood; (2) is seen as the result of the action of adrenalin; (3) occurs in diabetes mellitus and in pancreatic diabetes produced by experiment.

R. A. P.

**Ege, R.** Wie ist die Verteilung der Glucose zwischen den roten Blutkörperchen und der äusseren Flüssigkeit zu erklären? [**The distribution of glucose between the red blood corpuscles and the outer fluid.**] *Biochem. Ztschr.*, 1921, **114**, 88.

This is another contribution to the question of the permeability of blood corpuscles for glucose, in which the author confirms by a number of osmotic experiments the fact that the red blood corpuscles of the goat, ox, rabbit, and dog are impermeable for glucose. On the other hand, human blood corpuscles are permeable. A small amount of glucose is taken up at first and the rest slowly. The author thinks that a discrepancy between the results obtained from the method of the rate of permeability and of direct analysis is to be cleared up by considering the first amount of glucose as taken up (adsorbed) by the corpuscle wall. He is, however, emphatic on the question of the permeability of the corpuscle, and thereby contradicts the results of Falta and Richter-Quittner, who held that the permeability to glucose was only unmasked by the post-mortem treatment of blood and was not found in the presence of hirudin. R. A. P.

**Scott, E. L. Sugar in the blood of the dog-fish and the sand-shark.** *Am. J. Physiol.*, 1921, **55**, 349.

**Scott, E. L.**, and **Kleitmann, N. Sugar in the blood of the common frog.** *Ibid.* 355.

**SCOTT, E. L., and HONEYWELL, H. E. A study of the sugar in the blood of normal pigeons.** *Ibid.* 362.

The following data in different classes of vetebrates are of interest from a comparative point of view :

| | mgm. per 100 gm. of blood. | Remarks. |
|---|---|---|
| Dog-fish<br>Sand-shark | 65 | Great individual differences. Sugar may be completely absent. |
| Frog | 37 | In February, March, April. |
| Pigeon | 185 | High value corresponds to that found in other birds. |
| Dog<br>Cat | 65 | Given for comparison. |

W. C.

**SCHLOMOVITZ, B. H. Further experiments on the effects of warming and cooling the sino-auricular node in the mammalian heart. Depth of anaesthesia, tachycardia, flutter, sino-auricular heart-block. [B]. Experimental production of ventricular fibrillation by localized warming of cardiac tissue.** *Am. J. Physiol.*, 1921, **55**, 462, 485.

The sino-auricular node persists as the primary pace-maker of the heart even after long periods of ether anaesthesia. The stability of the position of the pace-maker indicates that the specialized tissue of the heart is as much an entity as the heart-muscle proper. A discussion of the pharmacological action of drugs must take into account the fact that the heart-muscle proper may be profoundly influenced with little or no effect produced in the specialized tissue.

Details are given of the experimental production of auricular flutter, ventricular fibrillation, and a tachycardia resembling certain cases of paroxysmal tachycardia. W. C.

**DE BOER, S. On the fibrillation of the heart.** *J. Physiol.*, 1921, **54**, 400.

After a brief discussion of the theories advanced to explain fibrillation, de Boer details experiments which he has made upon the frog's heart, using the string galvanometer. Fibrillation could be started by an extra stimulus in the shape of a single induction shock, provided that this is applied directly after the close of the refractory stage, and that the metabolic condition of the ventricle is bad. At this period in the heart's cycle the excitability of the muscle is slight, and a slowly travelling contraction with a brief refractory period is produced. The result is that when the contraction completes its circuit of the ventricle the muscle is again excitable, and the contraction can spread again and again round the heart. Fibrillation consists of a linking together of fractionated ventricular systoles.

O. L. V. de W.

**KIESSLING, W.** Vergleichende Untersuchungen über die Wirkung einiger Chlorderivate des Methans, Äthans und Äthylens am isolierten Froschherzen. **[Comparative experiments upon the effect of some chlorine derivatives of methane, ethane, and ethylene upon the isolated frog's heart.]** *Biochem. Ztschr.*, 1921, **114**, 292.

A series of methane, ethane, and ethylene derivatives have been compared with regard to their action in stopping the ventricle, in haemolysing red blood corpuscles, and in anaesthetizing the central nervous system. These properties do not run parallel. As an example: compared with chloroform, tetrachlormethane has a five times stronger effect upon the heart, and a ten times stronger haemolytic effect, while its narcotic effect is only one and a half times stronger. Aqueous solutions of chloroform, which have no effect upon the surface tension of water, have a powerful effect upon the heart, so that in this matter Traube's theory of narcosis is not supported. Frogs' hearts were used for these experiments. R. A. P.

**Bau, A.** Die Bestimmung der Oxalsäure und der Oxalursäure im Harn und im Kot. [**The determination of oxalic acid and oxaluric acid in urine and faeces.**] *Biochem. Ztschr.*, 1921, **114**, 221.

The paper describes at some length a method of estimating oxalic acid in urine and faeces. R. A. P.

**Hirai, K.** Über die Bildung von p-Oxyphenylessigsäure und p-Oxyphenylacrylsäure aus l-Tyrosin durch Bakterien. [**On the formation of paraoxyphenylacetic acid and paraoxyphenylacrylic acid from laevo-tyrosin by bacteria.**] *Biochem. Ztschr.*, 1921, **114**, 71.

Many workers have emphasized the importance of the exact conditions of a fermentation upon the products. In the present instance it is shown that a strain of *Proteus vulgaris* grown upon a protein-free medium containing the amino-acid tyrosin and a phosphate mixture, without the addition of glycerin, produces paraoxyphenylacetic acid. If glycerin is added, paraoxyphenylacrylic acid is formed. The time of the action of the bacteria on the medium is also found to influence the chemical composition of the final product. This type of work suggests the means by which the same bacillus in the body may produce different substances from the same chemical milieu under different conditions. R. A. P.

**Levene, P. A.**, and **Rolf, I. P.** **Lecithin. 4. Lecithin of the brain.** *J. Biol. Chem.*, 1921, **46**, 353.

The authors have re-opened, with the improved technique made available by their work, the question as to the presence of the phosphatide, lecithin, in the brain. This was considered to be present by the older workers, including the careful pioneer Thudichum. Fränkel and Linnert recently have denied the existence of it in the brain. The authors have been able to demonstrate satisfactorily that lecithin is a constituent of brain-tissue. They have also obtained indications that the brain may contain lecithins with more than one kind of fatty acid combined with them.
R. A. P.

**Sutherland, G. F.** **Contributions to the physiology of the stomach. LVI. Gastric secretions in starvation.** *Am. J. Physiol.*, 1921, **55**, 390.

In starvation there is a continuous gastric secretion which shows apparently spontaneous periods of more rapid secretion. W. C.

**Sutherland, G. F. Contributions to the physiology of the stomach. LVII. The response of the stomach glands to gastrin before and shortly after birth.** *Am. J. Physiol.*, 1921, **55**, 398.

Investigations on guinea-pigs, dogs, and cats, to determine the earliest capacity of the gastric glands to secrete hydrochloric acid during intra-uterine life and immediately after birth. W. C.

**Rehfuss, M. E.**, and **Hawk, P. B. Gastric analysis. I. Fundamental principles. II. The interdigestive phase or the principles governing the phenomena of the resting stomach.** *J. Am. M. Ass.*, 1921, **76**, 371 and 564. (*Physiol. Abstr.*, 1921, **6**, 136.)

The normal variations, especially in the direction of increased acidity, are considerable. The standardization of test meals is of the greatest importance. Secretion in the stomach is active even in the interdigestive phase. The interdigestive period reveals three phenomena. (1) Motor, in which peristole and tonal and hunger contractions supplant peristalsis. (2) Lessening in secretory activity with reduction of acidity to one-half. (3) An alteration in the status of the stomach and duodenum. In disease, the interdigestive phase may be completely obliterated. C. G. L. W.

**Kuramitsu, C.**, and **Loeb, L. The effect of suckling and castration on the lactating mammary gland in rat and guinea-pig.** *Am. J. Physiol.*, 1921, **56**, 40.

Detailed descriptions of the mammary gland in the conditions indicated in the title, without figures. W. C.

**Kuramitsu, C.**, and **Loeb, L. The involution of the uterus following labour, and the influence of castration and suckling on the process of involution.** *Am. J. Physiol.*, 1921, **55**, 422.

Nursing accelerates the involution of the uterus; lack of nursing weakens involution in both rat and guinea-pig. Castration intensifies involution. Involution of the uterus following labour takes a similar course in rat and guinea-pig; the changes take place with decreasing intensity and affect all the uterine tissues.

The effects of castration and of nursing are added to those of involution. These conditions merely change the intensity of the involution without altering markedly the time relations; the curves representing the involution under these various conditions take therefore a parallel course. Both castration and nursing affect all the principal constituents of the uterus, and they affect each tissue in an analogous manner; they influence the size of tissues, their proliferative activity, and their structure.

Castration and lack of nursing exert opposite effects. If they are combined, the effects of castration dominate. In castrated animals the effects of 'non-nursing' are much diminished and in the case of certain tissues suspended altogether.

In contradistinction to pregnancy, which in the guinea-pig not only suspends the ovarian cycle, but in addition and independently of the ovarian cycle inhibits the uterine cycle, lactation neither suspends the ovarian nor the uterine cycle. In the nursing rat, on the other hand, both are suspended.

While the cyclic changes which occur in the uterus of the nursing guinea-pig modify to some extent the effect of nursing on certain uterine tissues, the course of involution is approximately the same in these species, although they represent different types, as far as the effect of lactation on the periodicity of the sexual cycle is concerned.

The effects of nursing or the lack of it are in all probability exerted upon the uterine tissues directly and not indirectly by way of the ovaries. Castration seems to alter the uterine tissues in such a way that they become less responsive to the effects caused by the lack of nursing. W. C.

**Loeb, L.**, and **Kuramitsu, C.** **The influence of lactation on the sexual cycle in the rat and guinea-pig.** *Am. J. Physiol.*, 1921, **55**, 443.

There exists a marked difference between the behaviour of the rat and the guinea-pig as to the influence of lactation on ovulation and the sexual cycle. In the former, ovulation is suspended during the period of nursing, while in the latter it continues to take place. In the guinea-pig ovulation is followed in the nursing and in the non-nursing individual by the same cyclic transformation of the ovary. In the ovary of the rat ovulation is not followed by cyclic changes comparable to those of the guinea-pig. It may be suggested as a possible explanation of the difference found between the behaviour of the rat and guinea-pig, that in the rat the corpus luteum is functioning during a longer period of time than in the guinea-pig. W. C.

**van Dyke, H. B.** **A study of the distribution of iodine between cells and colloid in the thyroid gland. III. The effect of stimulation of the vago-sympathetic nerve on the distribution and concentration of iodine in the dog's thyroid gland.** *Am. J. Physiol.*, 1921, **56**, 168.

Various observers have concluded that the cervical sympathetic nerves have secretory control over the thyroid gland, because stimulation of these nerves produced an alteration in the iodine content of the gland. A careful investigation on the effect of stimulation of the cervical sympathetic failed to confirm these observations. W. C.

**Hammett, F. S.** **Studies of the thyroid apparatus. I. The stability of the nervous system as a factor in the resistance of the albino rat to the loss of the parathyroid secretion.** *Am. J. Physiol.*, 1921, **56**, 196.

This is a paper of exceptional interest. The author has removed in a very large number of rats (304) the parathyroids either alone or together with the thyroids. The rats used came from two stocks which had both been kept at the Wistar Institute in Philadelphia, where these experiments were carried out. One stock had for generations been petted and gentled and frequently handled. These rats were tame and not easily frightened. They give a uniform picture of placidity. The other 'standard stock' has had only that human contact incident to routine feeding and cage cleaning. These rats are timid, apprehensive, and high-strung; they object to being handled. The picture as a whole is one of constant instability and neuromuscular tension.

The standard stock gave a mortality from acute parathyroid tetany of 79 per cent., the gentled stock gave only a 13 per cent. mortality.

It follows that the condition of stability of the nervous system induced in these rats by petting produces in them a marked resistance to the loss of the parathyroid secretion which in excitable rats normally results in death from acute tetany in less than 48 hours. W. C.

**Stewart, G. N.**, and **Ragoff, J. M.** **Post-operative depletion of the epinephrin store of the adrenals.** *Am. J. Physiol.*, 1921, **56**, 220.

The post-operative depletion of the adrenalin load of the adrenals is due to the general anaesthetic, not to the trauma. It does not occur as a rule under local anaesthesia (ethyl chloride).

The adrenals of rabbits after thyro-parathyroidectomy were hypertrophied. The load of adrenalin was increased correspondingly, so that the weight of adrenalin per unit weight of gland was the same as in normal animals. The weight of adrenalin, if calculated per kilogram of body-weight was, however, distinctly increased after thyro-parathyroidectomy.
W. C.

**Adolph, E. F.** **The regulation of the water content of the human organism.** *J. Physiol.*, 1921, **55**, 114.

The water content of the body is not changed by taking pure water if the organism has been receiving previously its normal physiological supply. The excess water is very rapidly excreted. Diuresis due to water drinking is accompanied by a temporarily increased excretion of a few substances such as urea and chlorides, but this is compensated for by a lessened rate of excretion of these substances after the diuresis is finished. Hypotonic salt solutions are treated by the organism as mixtures of isotonic salt solution and water, the water in excess of that required for isotonicity being rapidly excreted. If isotonic salt solutions are given there is a definite retention of fluid and the haemoglobin of the blood shows evidence of dilution. Ingestion of salts or urea in hypertonic solution does not prevent diuresis by holding water in the body, but leads to moderate diuresis, the ingested substance being excreted in a concentrated form. Experiments were performed to show the effect of a dose of hypertonic NaCl solution on a diuresis following water ingestion, and conversely. After dehydration of the organism by sweating, work, low fluid intake, &c., ingested water was retained until the normal weight was restored. The reduction of the water content of the organism by these means did not lead to depletion of its salt content. No evidence was found for the presence of a reserve of free water in the body.
O. L. V. de W.

**Renauld-Capart, H.** Contribution à l'étude du métabolisme cérébral par la méthode des circulations partielles. 3. Recherche sur la nature des matériaux sécrétés par le foie nécessaires au travail des centres nerveux. [**The cerebral metabolism. 3. The nature of the substances secreted by the liver which are essential for the nervous centres.**] *Arch. internat. de physiol.*, 1921, **16**, 21. (*Physiol. Abstr.*, 1921, **6**, 122.)

The author has previously shown that exclusion of the liver from the circulation caused suppression of cerebral activity and death of the animal. The substance concerned in the function of the brain which is produced by the liver is not contained in the corpuscles. It is destroyed by a temperature of 57° C.–60° C. It is not specific, for both ox and dog's serum contain it, and the serum will resuscitate a dog deprived of its liver. It acts in small doses. It is a substance of the excito-secretory type, perhaps a ferment or catalyst. C. G. L. W.

**Dixon, W. E.**, and **Ransom, F.** **Immediate action of volatile substances.** *J. Physiol.*, 1921, **54**, 385.

The immediate action of alcohol, chloroform, ether, amyl nitrite, and other volatile substances administered by inhalation is the production of broncho-constriction. This phase lasts for about thirty seconds. Vaso-constriction is the initial effect of the same substances injected into the perfusion fluid of surviving organs, and also lasts about thirty seconds. The authors believe that this initial effect is due to the passage of the substance through the cells lining the vessels or bronchi. O. L. V. de W.

**Yamane, Jinshin.** Studien über die physikalische und chemische Beschaffenheit des Pferdespermas mit besonderer Berücksichtigung der Physiologie der Spermatozoen. [**The physical and chemical properties of horse semen in relation to the physiology of spermatozoa.**] *J. Coll. of Agricult., Hokkaido Imp. Univ.*, 1921, **9**, 161.

The author has made a very complete study of the properties of horse semen, and shows that it is a suitable test-object for determining the physiological qualities of solutions. The fluid contains, in addition to the usual constituents, some albumose. The author says it does not contain glucose. Repeated coitus within a short period reduces the amount of proteins in the fluid. The movements of spermatozoa are very resistant to bacterial invasion, so that semen which is in a somewhat advanced stage of putrefaction will still contain motile sperms. Some attention is paid to cluster formation by spermatozoa, which has been the subject of discussion by physiologists. He believes that it is due to a vital process connected with the electrolytes of the solution in which the sperms are suspended and is not due to agglutinins. The process does not occur with killed spermatozoa. Quickly repeated coitus does not influence the duration of life of the spermatozoa. Sperm may be very considerably diluted without affecting its capacity for insemination. While the author refers to the effect of hydrogen ions on the motility of spermatozoa, no attempt was made throughout the investigation to control this important factor, and many of the experiments lose much of their value on this account. C. G. L. W.

**Flu, P. C.** **The period during which *Stegomyia* can live at low temperatures.** *Med. u. het Geneesk. Lab. te Weltvreden, Java*, 1920, **3**, ser. A, 495. (*Physiol. Abstr.*, 1921, **6**, 115.)

The investigation arose from the question of storage and transport of fruit in refrigerators and the possibility of infection from mosquitoes which might also be stored. If the temperature does not rise above 6° C. *Stegomyia* dies within 24 hours. Between 7° C. and 10° C. they die in four days.

C. G. L. W.

**TRÖNDLE, A.** Neue Untersuchungen über die Aufnahme von Stoffen in die Zelle. [**New experiments on the uptake of substances by the cell.**] *Biochem. Ztschr.*, 1920, **112**, 259.

The experiments in this paper were designed to show that the living cell participates actively in the uptake of substances from the surrounding medium. This intervention of the cell differs according to the substance taken up. In the ordinary way the amount of KCl or NaCl taken up by such cells as the palisade cells of *Buxus sempervirens* is constant and independent of the concentration outside. Narcosis with ether or chloral hydrate depresses the uptake of salts by the cell, though the typical permeability relations are re-established after a time.

The effect of dilute acids is different. They raise the permeability of the cell and establish conditions in which Fick's diffusion law is obeyed between the inside and outside of the cell. Experiments were further made upon the penetration by alkaloid bases of two species of spirogyra; the alkaloids used were quinine, caffeine, and piperidine. The penetration was found to obey Fick's law in this case. Salts of the alkaloid bases took longer to penetrate. The addition of a trace of acid to depress the dissociation of the salts inhibited penetration altogether. This confirms an opinion of Overton that the penetration of the alkaloid salts is governed by the amount of free base hydrolytically dissociated. However, cells suspended in solution of the alkaloid in the state of base, salt, and salt plus acid to which chloroform has been added, die in the same time. This, in the opinion of the author, confirms the view that the entry of substances into the cell is governed by the living protoplasm. R. A. P.

**FENN, W. O. The phagocytosis of solid particles. I. Quartz. II. Carbon.** *J. Gen. Physiol.*, 1921, **3**, 439.

The chances of collision between leucocytes and quartz particles of different sizes can be calculated and the experimental rate of ingestion is found to be in accordance. A verification is provided by varying the speed of rotation of the tubes. Similar results were obtained with carbon particles. Phagocytosis of carbon is nearly absent unless serum is present. The clumping of unwashed leucocytes is accelerated by serum and by ingestion of carbon. The phagocytosis of bacteria does not follow the law for unimolecular reactions. W. M. B.

**FREUDENBERG, E.**, u. **GYÖRGY, P.** Über Kalkbindung durch tierische Gewebe, II. [**On calcium combination with animal tissues.**] *Biochem. Ztschr.*, 1921, **115**, 96.

The experiments deal with differences in the behaviour of various forms of cartilage to suspension in $CaCl_2$ and other solutions. Calves' cartilage and human cartilage take up Ca from Ca solutions, whereas the cartilage of infants takes up practically no calcium from solutions of calcium acetate or nitrate. Other anions are also bound by cartilage, the series in order of effectiveness being Mg, Ca, Sr, Ba, Al. When cartilage is put into mixtures of Ca and Mg, the one ion inhibits the combination of the other ion. Ca acts more powerfully against Mg in this respect than Mg against Ca. Brain takes up Mg more strongly than Ca, but Ca inhibits Mg even in small amounts. The author has been able to get a physical analogy for these experiments out of the behaviour of gelatin solutions and relates them to problems of Mg narcosis. R. A. P.

**Pighini, G.** Chemische und biochemische Untersuchungen über das Nervensystem unter normalen und pathologischen Bedingungen. VIII. Beitrag zur chemischen Zusammensetzung des Gehirns bei ‘ Dementia Praecox ’. [**Chemical and biochemical experiments on the nervous system under normal and pathological conditions. VIII. Study of the chemical composition of the brain in dementia praecox.**] *Biochem. Ztschr.*, 1921, **113**, 231.

An analysis of the chemical composition of the brain in dementia praecox shows the following changes. There is an increased amount of water present, a decrease of from 20–35 per cent. in the unsaturated phosphatides and a decrease of about 50 per cent. in the saturated phosphatides (cerebroside, &c.). There is also a slight increase in the protein residue. R. A. P.

**Feigl, J.** Zusammensetzung der Leber bei akuter gelber Atrophie. [**Composition of the liver in acute yellow atrophy.**] *Biochem. Ztschr.*, 1921, **115**, 21.

Chemical analyses have been made of 24 cases of acute yellow atrophy of the liver. The results obtained are on the whole difficult to summarize. In many cases, though not in all, there was an increase in the percentage of water, with a corresponding decrease in the amount of fat. Amino-acid seems as a rule to be a good deal increased. Cholesterin content is apparently very variable. R. A. P.

**Magnus, R.** Cholin als Hormon der Darmbewegung. [B.] [**Choline, the hormone of intestinal peristalsis.**] *Die Naturwissenschaften*, 1920, Heft 20.

In this review Magnus gives the results of his own and other investigations on the pendulum and peristaltic movements of the intestines.

He discusses the mechanism whereby the nervous system of the Auerbach plexus initiates rhythmic movements of the intestine, and comes to the conclusion that it must be due to a chemical stimulus. A search for the substance showed that it was heat-stable, and diffused out of the intestine into the medium in which the intestine was suspended. Further investigation showed that treatment of the solution with acetic acid produced a much more active agent, which indicated that the substance had certain analogies with choline, which has been studied by Reid, Hunt, and Dale. It has been possible to isolate the substance and identify it, and it proves to be choline itself.

The intestine possesses specific ferments which are able to synthesize acetyl and pyruvyl choline when acetates and pyruvates are present, and the peristaltic action of the salts is due to this fact. Magnus points out that the extracts of the uterus act in the same way as those of the intestine. It is possible here also that the rhythmic contraction of the uterus is in part initiated by this compound. C. G. L. W.

**Lüers, N. A general colloid test in cerebrospinal fluid and the use of Congo-rubin.** *Kolloid-Ztschr.*, 1920, **27**, 177. (*Physiol. Abstr.*, 1921, **6**, 32.)

A general discussion of the use of gold sols and mastic sols as an aid to diagnosis of certain pathological conditions of the cerebrospinal fluid. The author suggests that the Congo-rubin sol might constitute a valuable reagent for this purpose, since it is more easily applied than either of the other sols. The method consists in measuring the protecting action of the colloids in the fluid on the colour change brought about by potassium chloride. Three samples of cerebrospinal fluid were examined. The method consisted in mixing 1·0 c.c. of 0·1 per cent. Congo-rubin solution with 1·0 c.c. of the fluid, adding 7·65 c.c. of distilled water and 0·35 c.c. of saturated potassium chloride solution, and measuring the time taken for the colour change to occur. With normal healthy fluid 41 seconds were required, in the case of locomotor ataxia 66 seconds, and in a case of syphilis 110 seconds. C. G. L. W.

**Epstein, J. W. Intra-peritoneal administration of sodium bicarbonate solution.** *Arch. Pediat.*, 1920, **37**, 656. (*Chem. Abstr.*, 1921, **15**, 901.)

A solution of 5·0 per cent. sodium bicarbonate may be used as an intraperitoneal injection, but a 2·0 per cent. solution isotonic with the blood is preferable. The percentage of recoveries in the acidosis of children when this method is employed is unusually high. Fatal cases do not show any pathological effects due to the salt. C. G. L. W.

**Warburg, O.**, u. **Negelein, E.** Über die Oxydation des Cystins und anderer Aminosäuren an Blutkohle. [**On the oxidation of cystin and other amino-acids by blood charcoal.**] *Biochem. Ztschr.*, 1921, **113**, 257.

Recent work is tending to emphasize the importance of the surface in many reactions occurring in the living cell. The work here is concerned with the effect of blood charcoal upon amino-acids. In the presence of blood charcoal, the amino-acids cystin and cystein can be oxidized quantitatively to $CO_2$, $H_2O$, $NH_3$, $SO_3$. Leucin and tyrosin are converted to $CO_2$, $H_2O$, and $NH_3$ R. A. P.

**Doerr, R.** Zur Oligodynamie des Silbers. [**On the oligodynamic action of silver.**] *Biochem. Ztschr.*, 1921, **113**, 59.

The effect of extremely small traces of the heavy metals such as silver, the so-called oligodynamic action, is of great interest. It has been known since the time of Nägeli that the insertion of a copper rod into glass-distilled water is sufficient to render the water toxic to tadpoles, though the amount dissolved is infinitesimal. The author has been studying this effect with silver upon the growth of bacteria. He has found that the heating of the silver first in a Bunsen flame renders it non-toxic when inserted into a solution. In some way the toxic compound is formed upon the surface. It seems to be connected with oxidation, because the toxicity can be regenerated by letting the heated silver remain in the air.

There is a difference between the behaviour of growing colonies of the typhoid, paratyphoid A, and B bacilli on the one hand, and those of the coli group on the other. The former are able to develop in a greater concentration of silver than the latter. The difference is accentuated by the addition of lactic acid. It is claimed that this can be used as a method of isolation. R. A. P.

# RADIOLOGY AND ELECTROLOGY

## *Radio-diagnosis*

**Försell, G. A few notes on the diagnosis and differential diagnosis of tuberculosis in bones and joints.** *Arch. Radiol. & Electroth.*, 1921, **25**, 247 and 293.

The author states that the principal object of an X-ray examination is usually to establish the localization, extent, and intensity of the tuberculous change and to observe its course. Sometimes, however, X-rays may help in diagnosis. With experience the changes in density of the plate will afford much information; early cases may not show any such changes, since, if the disease has not caused a visible change in the normal percentage of mineral matter, no change is seen in the radiogram. If there is great decrease in the density of the bone the plate may be over-exposed and large destructions then may be invisible. In these cases soft tubes with sharp focus must be used and photographs taken with a small diaphragm in several different directions.

From the descriptions of twenty-two plates of tuberculous joints the following are the most important points: localization of the bone foci, chiefly to the epiphyses; destruction without any repair in the progressive stages; the round shape of the epiphyseal foci; 'vitreous atrophy'; reduction of articular cartilages; erosion of the bony surfaces; thickening of the articular capsule; the presence of abscess shadows. The findings must be considered as a whole and caution must be used before returning a negative report.

The author then describes the differential diagnosis between tuberculous disease of bones and joints and the following: Köhler's disease, Legg's disease, Schlatter's disease, osteochondritis dissecans, traumatic arthritis, acute osteo-myelitis, bone abscess, congenital and gummatous disease of bone, gout, enchondromata, osteitis deformans, secondary carcinoma in bone, sarcoma of bone, fractures through the epiphysis or epiphyseal cartilages without dislocation in young children. In conclusion, he states that the value of a radiogram depends on the perfection of the technique. The paper is illustrated by numerous excellent plates. P. L.-B.

**Mouchet, A.** Ostéo-chondrite déformante infantile de l'épiphyse supérieure du fémur. [**Infantile osteo-chondritis deformans of the upper epiphysis of the femur.**] *Bull. et mém. Soc. de chir. de Par.*, 1920, Dec. 8. (*Arch. d'électric. méd.*, 1920, **28**, 362.)

In connexion with some work by M. Sorrel, the author studied an affection of the hip-joint distinguished from coxalgia. The clinical symptoms in this condition are nothing compared with the radiological which shows the following:

(1) Head of the femur. Often fragmented, very flattened, with zones of decalcification.

(2) Epiphyseal cartilage. Irregular, notched, and broken up into small islets.

(3) Neck of the femur. Is markedly thickened; sometimes coxa vara sometimes coxa valga.

(4) Epiphyseal line. Appears thickened, probably due to an intra-articular effusion.

(5) Cotyloid notch. Shows irregularities, an important characteristic, disregarded by most authors.

The condition lasts about a year; it does not end in a destruction of bone, an abscess, or ankylosis. It has a natural tendency towards recovery. It is probably a question of an epiphyseal osteitis of growth.

P. L.-B.

**Dobreuilh** et **Bardet**. Difformités des mains causées par des cicatrices datant de l'enfance. [**Deformities of the hands since childhood caused by cicatrices.**] *J. de méd. de Bordeaux*, 1920, Aug. 25, 431. (*J. de radiol. et d'électrol.*, 1920, **4**, 518.)

The authors report two interesting cases. The first is that of a woman of 63, suffering from a deformity of the right hand due to a burn when five years old. The forearm ends in a large stump, from which hangs a mass the size of a small orange; this represents the hand. An X-ray photograph shows the details of this marked deformity well. It shows the metacarpo-phalangeal or interphalangeal articulations more or less subluxated; distal phalanx of the thumb is greatly reduced in size; the little finger is hidden behind the others; the two distal phalanges of the index finger are united and two small exostoses are seen. The curvature of the metacarpals and of the first phalanges is greatly exaggerated. The radius and the ulnar are very small.

The second case is that of a woman of 30, suffering from tuberculosis of bone and skin since childhood. Great deformity of the hands and a superadded epithelioma of the left wrist of two months' duration. If only a superficial examination were made one would conclude that the majority of the bones of the left hand had disappeared. That, however, is not the case, and an X-ray photograph is surprising; the skeleton is almost complete, only the distal phalanx of the little finger is completely absent. The first phalanx of the thumb is reduced to a small round mass. The bones of the middle, ring, and little fingers are very small and in the most extraordinary positions. The radius and ulnar are also very small. On the right hand the absence of the index finger is noted; the metacarpal, greatly curved, alone remains.

P. L.-B.

**Chicaudard, M.** La tuberculose du calcanéum chez l'enfant. [**Tuberculosis of the calcaneus in children.**] *Thèse de Paris* 1920. (*J. de radiol. et d'électrol.*, 1921, **5**, 82.)

In this work, based on a hundred cases, the author, in the course of a general and thorough study of tubercular osteitis of the calcaneus, gives from the radiological point of view, which concerns us especially, some interesting information.

I. **Normal radiograph.** As regards technique the author repeats the necessity of making a comparative examination of both feet, and of taking three plates of each, two plates from the front, the first as for the tibio-tarsal joint (foot at a right angle to the leg, normal ray passing through the tibio-tarsal articulation), the second as for the sole of the foot (foot flat on the plate) but centring on the anterior tibio-tarsal articular junction. A projection of the calcaneus is obtained, partly hidden by the astragalus, but the posterior end can be clearly seen. The third plate, from the side, gives the greatest information. From the lateral radiograph of a normal foot the author draws some interesting measurements to which the reader should refer in the text and which allow comparisons to be made between the picture of the normal foot and that of the pathological.

II. **Pathological radiograph.** (i) Stage of onset: (*a*) Decalcification, often extending to all the bones of the tarsus and the distal end of the tibia. (*b*) Hyperosteogenesis, sometimes so marked that the primitive point of ossification on the affected side exceeds by a third or a half the size of the corresponding point on the sound side and that the epiphyseal centre in the posterior part of the calcaneus and the points of ossification almost (cuboid and scaphoid) appear before their homologues on the sound side. (ii) Stage of actual disease: (*a*) Massive infiltration—a rare form—with a soft appearance and greyness of the whole calcaneus. (*b*) Nodular infiltration, more frequent, denoted by a clear spot, the cavity, of varying size, possibly taking up almost the whole bony nodule. If there be extension to the neighbouring joints, adhesions in the joint cavities can be seen. (iii) Stage of repair: On the plate is seen the appearance of sclerosing osteitis—that is to say, the recalcification of the healthy parts with the exception of the clear space, in the middle of which a sequestrum is seen. Fistulae can only be revealed by opaque injections. (iv) After treatment, determined by the appearance of sclerosing osteitis, radiography affords assistance in all stages of repair of the bone in the course of which can be seen the filling up of the operation cavity, by tissue at first fibrous, subsequently replaced by bony arches, the last stage of restitutio ad integrum. P. L.-B.

**Mouchet, A.** La scaphoïdite du tarse des jeunes enfants (dite maladie de Köhler). [**Inflammation of the tarsal scaphoid in young children (Köhler's disease)**]. *Bull. et mém. Soc. de chir. de Par.*, 1920, April 14. (*Arch. d'électric. méd.*, 1920, **28**, 316.)

With the help of three observations, one by Roederer and two by himself, the author describes this affection, which was known in Germany before the war. Having, so to speak, no symptomatology, it draws its interest and originality from the radiographic image. Only thirty cases have been published up to the present time.

The affection shows itself between the ages of five and ten. The child, without any signs of rickets, and without hereditary or personal antecedents, suffers all at once in the scaphoid region; possibly he thinks he has twisted his foot, or has knocked it against some obstacle. Lameness is slight, varus or valgus. Pain does not cease during rest; the scaphoid region is swollen (soft parts or the bone itself) and is painful on pressure. The affection is generally unilateral, but when both feet are attacked it is always one after the other. Radiography, which is the only means of diagnosis, shows the following modifications of the bone: it has become thinner and greatly flattened, with irregular, denticulated contours; it is condensed, the cortical and spongy parts are intermingled, its opacity is metallic, and sometimes it has a dappled appearance.

The malady has a natural tendency towards cure. Relapse is rare after rest and immobilization. Cure takes from eighteen months to two years. After this period radiography shows the bone to be normal in density, form, and dimensions.

The nature of this inflammation of the scaphoid in young children has been much discussed, but only two French observations thereon have been published. It is certain that neither tuberculosis nor syphilis plays a part in it. Köhler allows it to be an anomaly of development; others consider it a fracture by compression: Preiser speaks of a trophic disorder consequent upon damage done to the nutrient vessels of the bone by even the smallest injury. Mouchet inclines to the opinion, from his radiographic examinations, that it is caused by fracture, but by fracture prepared by dystrophy of the bone, particularly predisposed by its rôle of key-stone of the arch of the foot. He thinks many cases must have escaped clinicians, especially those 'who have not the firm faith in radiography which we all ought to have'. S. U. L.-B.

**McClure, C. W., and McCarty, E. D. Roentgenographic studies in gout.** *Arch. Int. Med.*, 1919, **24**, 563. (*Arch. d'électric. méd.*, 1920, **28**, 316.)

The authors, after having studied the osteoarticular lesions of gout, came to the conclusion that the presence of very limited osseous foci, whose density was much diminished because of the disappearance of the calcium salts, was a characteristic sign of a gouty lesion; a similar change not taking place in chronic rheumatism. But, Strangeways having produced observations contrary to this conclusion, they studied the question afresh on nine clinical cases of true gout, and on 100 cases of chronic rheumatism. In their opinion, examination of the plates show:

(1) Foci of osseous rarefaction, especially clear at the level of the heads of the metacarpals and metatarsals.

(2) Besides these foci, light notches on the extremities of the articular surfaces at the level of the first metatarso-phalangeal articulation.

(3) Possible decalcification of all the bones of the affected member or simply of those whose articulation is interfered with.

(4) Sometimes a certain contracture of the spaces, with proliferative or atrophic lesions. All these lesions, however, only concern certain joints, others remain intact.

In one type of chronic rheumatism they found proliferative lesions on the edges of the articular surfaces, without noticeable osseous atrophy; in a second type, a certain generalized osseous atrophy without destructive lesions of the articular surfaces, followed by a fusiform thickening of the soft periarticular parts; in a third, concomitance of proliferative lesions and osseous atrophy.

From these conclusions it may be seen that the presence of bony atrophy is not a characteristic sign of gouty lesion, although this change may exist in gout alone in the absence of every other osteoarticular lesion. It should rather be said that it is the absence of this change, which is almost constantly found in cases of gout in the bones of the wrist, hand, tarsus, and of the foot, that has a certain diagnostic value.

S. U. L.-B.

## *Radiotherapy*

**Manoukhin, I. I. The treatment of infectious diseases by leucocytolysis produced by röntgenization of the spleen.** *Lancet*, 1921, i. 685.

The author states that an organism combats infection chiefly by the breaking up of its leucocytes, and that the cure is brought about owing to the fact that the specific antisubstances produced by the leucocytes are set free by leucocytolysis. The process is effected by soluble ferments which he proposes to call 'leucocytolysins' and the leucocytosis is caused by other ferments called 'antileucocytolysins': the former are, according to M., produced by the spleen and the latter by the liver. Monkeys and guinea-pigs were inoculated with human tubercle bacilli and the spleen was artificially stimulated by X-rays.

**Method of radiation.** The spleen in man is radiated by a dose of X-rays equal to 1 h. by the Sabouraud and Noiré radiometer, using the Holzknecht scale; 1 mm. aluminium filter is used. In monkeys and guinea-pigs the dose is somewhat less and softer rays are used. The liver must not be radiated as the ferments secreted by it are antagonistic to those of the spleen. X-rays applied to the spleen increase the proportion of complement, haemolysins, agglutinins, bacteriolysins, and opsonins in the blood. From experiments on guinea-pigs inoculated with human tubercle bacilli the author was convinced that the curve of fluctuation of specific antisubstances in the blood corresponded to the curve of fluctuations of the leucocytolysins.

From the experiments on animals the author proceeded to X-radiate the spleen in patients suffering from various infectious diseases. Tuberculosis was first treated in 1913. Typhoid was treated during the war, and by röntgenization of the spleen the mortality was reduced to one-half. The treatment was supplemented by feeding the patient with an autoserum taken 8–10 minutes after the application of the X-rays, and by this means the mortality was reduced 7½ times. Tetanus also was treated by this method, with the result that in 132 cases the mortality was only 27·3 per cent. X-ray applications to the spleen were also used for the preparation of antisera at the same time that horses were being immunized against tetanus, typhoid, dysentery, and cholera.

The author states that many other acute infectious diseases such as pneumonia do well after one application of X-rays, and he also mentions some non-infectious diseases which can be successfully treated by this method. Dysentery, chiefly the Flexner type, is stated to be very favourably influenced by the introduction of autoserum into the large intestine through a long syringe.

**Pulmonary tuberculosis**: in the last seven years 8,000 cases have been treated in most unfavourable climatic conditions. Radiation is not carried out more than once a week; according to the stage of the disease the séances varied from 8–15; in the third stage two series were generally given at intervals of 2–3 months. The disease treated in the first stage improves at once; in second stage the patients become slightly worse at first; the third stage responds like the second. **Tuberculosis of the kidneys and bladder** usually do well with 15 séances. **Tuberculosis of lymphatic glands** is treated in the same manner as kidney cases; if suppuration has occurred it is treated surgically. **Tuberculosis of bone** is treated by 15 séances. **Tuberculous peritonitis** generally progresses satisfactorily; no details are given as to the number of séances. **Tuberculous meningitis**: only acute cases do not yield to this form of treatment; it is suggested that autoserum from the first might be of use.

The author concludes by stating that röntgenization of the spleen brings in nothing new, but strengthens Nature's defensive mechanism, and that by its means radical help can be given to a patient suffering from an infectious disease. P. L.-B.

**Frieberg, F.** 3 fall av radiologiskt behandlad hypofystumor. [**Actinotherapy in three cases of tumour of the hypophysis.**] *Hygeia*, 1921, **83**, 63–5.

Of Frieberg's three cases, the first was that of a woman of 52, whose ocular symptoms, as well as the X-ray findings, indicated a tumour in the region of the hypophysis. A negative Wassermann and the failure of repeated courses of mercury to effect improvement excluded the diagnosis of syphilis. Röntgen and radium treatment were prescribed, and on four occasions marked improvement of vision was observed within a few days of an exposure. The second patient was a man, aged 46, who also responded well to combined treatment with X-rays and radium. The third case was less instructive because syphilis could not be definitely excluded, and the improvement effected could not be wholly dissociated from the antisyphilitic treatment instituted. C. L.

**Walterhofer, G.** Über die Einwirkung der Röntgenstrahlen bei Leukämie. [**The action of X-rays in leukaemia.**] *Berl. klin. Wchnschr.*, 1920, **57**, 581. (*J. de radiol. et d'électrol.*, 1921, **5**, 137.)

The reason for the brilliant but never definitive successes obtained from the use of radiotherapy in cases of leukaemia is to be found in the elective sensibility of the white cells and of the leucopoiëtic tissues when exposed to X-rays. Three phases may be distinguished in the changes which occur during irradiation. The first is characterized by the capricious oscillations of the number of the leucocytes, which applies to all varieties of white cells. After a short rise in the number of leucocytes, which occurs immediately after application of the rays, a decrease of up to 100,000 cells per c.mm. takes place in a few hours, and is followed again by an increase. These variations appear to be due to local variations in distribution of the white cells. The second phase is marked by a constant decrease in the number of the leucocytes. These are affected variously according to the type of the disease, but the tendency of the blood-formula is to approach the normal, while being always distinguished by the presence of some myelocytes, an increase in the number of the mast cells, and by signs of immaturity of the nucleus of the polynuclears.

The third phase is characterized by a return to the leukaemic formula, which becomes evident first by multiplication of the myelocytes without notable increase in the number of the white cells, then by reappearance of the myeloblasts.

In lymphatic leukaemia, diminution is only observed in the number of lymphocytes, often associated with a decrease of the already scarce polynuclears.

The red cells and the haemoglobin, after a fleeting diminution, increase and even surpass the normal, and at the same time the nucleated forms disappear.

The mechanism of these cellular changes has only been imperfectly elucidated. The destructive action of X-rays is well established and is confirmed by the exaggerated excretion of nitrogen and of uric acid formed at the expense of the nucleins destroyed during the period following irradiation; this excretion should enable one to judge of the efficacy of the treatment. S. U. L.-B.

**Schlecht.** Die Röntgentiefentherapie in der inneren Medizin. [**Deep radiotherapy in internal medicine.**] *München. med. Wchnschr.*, 1920, **67**, 800. (*J. de radiol. et d'électrol.*, 1921, **5**, 136.)

It would be dangerous to employ in divers medical affections the intensive method of radiotherapy, the entire dose in one séance, which has given excellent results in gynaecology. The author prefers a series of smaller applications given at intervals. The different affections for which treatment by X-rays is beneficial, lymphadenomata, granulomata, lymphosarcomata, mediastinal tumours, certain forms of tuberculosis, Basedow's disease, neuralgia, &c., need different doses. The author here confines himself to the technique used in the treatment of myeloid leukaemia. The region of the spleen is divided into as many areas of 10 sq. cm. as is necessary (from 6 to 12), which are irradiated from the back or abdominally. Two areas are irradiated per day with a Sabouraud dose, filtered by 4 mm. aluminium. The series, which takes from 4 to 7 days, is recommenced after 15 days, the condition of the blood being examined. The number of leucocytes and the volume of the spleen should be reduced very slowly, and treatment should be stopped when the general state of the patient is improved, provided that the percentage of haemoglobin does not decrease. The doses may be carefully increased by half, then doubled, until the desired result is obtained, by spacing the series from 3 to 4 weeks. The blood is examined every 6 weeks and according to its condition treatment is suspended or resumed. By these means the author had a patient under his care for 8 years. He considers that the X-rays must be used as a medicament and that rapid results, brilliant to all appearance, are most often dangerous and to be mistrusted. S. U. L.-B.

## *Radiobiology*

**Cramer, W., Drew, A. H.,** and **Mottram, J. C. Similarity of effects produced by absence of vitamines and by exposure to X-rays and radium.** [**B**]. *Lancet*, 1921, i. 963.

The authors state that, from the fact that the complete absence of vitamines is incompatible with maintenance of life in the higher animals, it is generally assumed that vitamines are essential for the life of the cell. They do not agree with this, since in animals kept on a vitamine-free diet the adrenals hypertrophy, as they do in chronic starvation. They state that vitamines are essential to the maintenance of life as a whole in a highly differentiated animal, but not necessarily, or probably, of its individual cells. Lymphoid tissue, however, is profoundly and specifically affected by lack of vitamines; in animals kept on a vitamine-free diet the lymphoid tissue throughout the body atrophies markedly: the blood picture shows a reduction in the number of lymphocytes and an increase in the number of polymorphonuclears. These conditions can be produced by appropriate doses of X-rays or radium, after which the animals also lose weight and die in an emaciated condition. The results show that the lymphoid tissue has a greater effect upon the nutrition of the body than is generally realized, and possibly the lack of vitamines and radium or X-rays produce their effects mainly by acting on this type of tissue. The authors propose to make further investigations as to why two such dissimilar causes should produce the same effects. P. L.-B.

**Murphy, J. B., Nakahara, W., Hussey, R. G., Sturm, Ernest. Effect of the cellular reaction induced by X-rays on cancer grafts.** *J. Exper. M.*, 1921, **33**, 299.

This paper contains the results of experiments upon the fate of cancer grafts, namely, grafts of an adenocarcinoma of the mouse, when the region of the body into which the graft is inoculated is previously exposed to X-rays. The rays used were of an easily absorbed type, the alternative spark-gap of the X-ray bulb being ¾ inch.

Experiments were made by exposing limited portions of the surface of the body of the mouse to the rays and then inoculating grafts into these regions—the grafts were inserted either intra- or sub-cutaneously; microscopic and macroscopic observations were then made of the subsequent fate of the tumour grafts with the following results:

Small areas of the skin in the groin of mice were subjected to an erythema dose of X-rays and a week later a cancer graft was inoculated intracutaneously into the area, and at the same time a like graft was inoculated in the same manner in the opposite groin protected from X-rays. The graft in the X-rayed area showed a low percentage of takes, while that in the normal skin gave the usual high percentage. When the graft was introduced into the subcutaneous tissues it grew equally well in the X-rayed area as in the protected area.

Histological examination shows the skin layers, a few days after X-ray treatment, to be markedly infiltrated with round cells of the lymphoid type. The reaction did not extend deeper than the skin layers. It is suggested that this local lymphoid reaction induced by the X-rays controls the graft made into the skin, while its absence in deeper tissues accounts for the growth of the grafts more deeply implanted. S. R.

**Murphy, J. B., Hussey, R. G., Sturm, E., Nakahara, W. Effect of induced cellular reaction on the fate of cancer grafts.** *J. Exper. M.*, 1921, **33**, 315.

The authors first show that mice develop an enhanced refractory condition to the growth of transplanted tumour (adenocarcinoma) if they are first sensitized with rat blood and inoculated ten days later with a mixture of rat blood and mouse tumour. This immunity is not apparent if the rat blood be omitted in this test inoculation. Finding that there was evidence of a lymphoid reaction supervening upon the first sensitization, the authors sought to modify the subsequent degree of immunity by a suppression of this lymphocytic activity by means of suitable doses of X-rays; this was successful to some extent though not completely.

The authors draw particular attention to the fact that the condition of local anaphylaxis renders the tissues affected unsuitable for the growth of a cancer graft, and further that the histological changes which arise correspond with those seen round a cancer graft in an animal immunized by a previous injection of homologous tissue—for instance, mouse blood.

The mode of action of the X-rays in the suppression of the refractory state is discussed by the authors, who are inclined to refer it to a suppression of the cellular exudate of the participating tissues. S. R.

**Murphy, J. B., Nakahara, W., Sturm, E. Relation between the time and extent of lymphoid stimulation induced by physical agents and the degree of resistance to cancer in mice.** *J. Exper. M.*, 1921, **33**, 423.

These experiments are a continuation of the author's work on the association between lymphoid activity and resistance to cancer inoculation in mice. The two modes they employ to effect a lymphoid stimulation are subjecting the mice either to small doses of X-rays or to dry heat. The phases of lymphoid activity following either procedure have been studied by the authors, and have been shown to be of a complex nature.

By injecting the mice with portions of tumours at different times corresponding to the phases of lymphoid activity, the authors found a certain degree of parallelism to exist between the degree of immunity and that of lymphoid activity.

This lymphoid activity cannot, however, be gauged by the number of lymphocytes circulating in the blood-stream, for it has been shown by other observers that animals having extremely high lymphocytic counts may exhibit no appreciable immunity, and, on the other hand, an immune animal may have no more than the average number of lymphocytes shown by the normal animal. S. R.

**Nakahara, W., and Murphy, J. B. Effect of small doses of X-rays of low penetration on the resistance of mice to transplanted cancer.** *J. Exper. M.*, 1921, **33**, 429.

The effect of a single dose of X-rays upon mice was tested as to its action upon the resistance of the animals to a subsequent inoculation of tumour (adenocarcinoma).

The interval between the irradiation and the inoculation was varied from three to seven days, but there was no close association between the degree of resistance induced by the X-rays and the interval between irradiation and inoculation. In all cases, however, there was evidence of less growth of the tumour in the mice which had previously been given a dose of X-rays. This degree of immunity was in no case absolute, and the amount of added resistance which it is possible to give an animal by this means appears to depend very much upon the degree of virulence of the tumour used for the purposes of the test. S. R.

**Nakahara, W., and Murphy, J. B. Influence of cancer inoculation on the lymphoid stimulation induced by small doses of X-rays.** *J. Exper. M.*, 1921, **33**, 433.

Mice treated with small doses of X-rays and inoculated with cancer immediately afterwards, show a marked suppression of lymphoid proliferation.

If, however, the cancer inoculation is made seven days after the exposure to X-rays, thus permitting the primary lymphoid stimulation known to occur soon after the X-ray treatment to arise, a second stimulation takes places in a large proportion of mice thus inoculated.

Changes in the blood of mice X-rayed and inoculated with cancer seven days afterwards show that the state of resistance to cancer inoculation is attended by a lymphocytosis, as is the case in all other varieties of immunity to transplanted cancer so far studied. S. R.

## *Electrodiagnosis.*

**Neri, V.** Importance séméiologique de l'examen électrique de la sensibilité cutanée. [**The semeiological importance of electrical examination of cutaneous sensibility.**] *Rev. neurol.*, 1920, **i**, 19. (*J. de radiol. et d'électrol.*, 1921, **5**, 45.)

As a means of examining the cutaneous sensibility, electrical stimulation is better than all others because it can be more easily and more accurately applied and measured; thanks to it, alterations which because of their smallness would be liable to be unobserved can be ascertained, and the progression or retrogression of an ascertained alteration in sensation can be accurately followed. Electrical examination of the cutaneous sensibility should be made both with the faradic and galvanic stimuli.

I. **Electrical examination of the sensory organs.** The examination is made by the unipolar method: the large indifferent electrode on the back, the active electrode on the particular cutaneous surface. In the faradic current, the best active electrode is Erb's, made of a bundle of more than four hundred fine metallic wires. Painful sensations should not be obtained. In cases of unilateral disorders the value of the research lies entirely in the comparison of the sound with the injured side. The zones of alteration of painful sensation to faradism (hyperaesthesia, anaesthesia, hypaesthesia) are usually more extensive than the zones of alteration brought to light by the other stimuli (Carati). This same author has found a difference between the faradic stimulus and the other cutaneous and painful stimuli: faradic hypaesthesia in the zones of tactile hyperaesthesia and pain.

The author has proved in tabes a noticeable degree of farado-cutaneous hypaesthesia associated with a very pronounced galvanic hyperaesthesia; this difference had already been observed, and demonstrates the necessity of following the research on the faradic sensibility by that on the galvanic sensibility.

With an equal current, it is the rule that the painful sensation is more pronounced at the closing of the cathode than at the opening of the anode. It is possible to have equality of polar sensation or inversion of polar sensation.

II. **Electrical examination of the sensory nerves.** It is of the greatest importance. Unipolar method: indifferent electrode on the back, active electrode on the sensory nerve. The author, instead of placing the stimulus on the mixed nerves, stimulates the cutaneous nerves at their point of emergence from the aponeuroses. In analogy with the motor points, he calls these points of election 'sensory points'. At the time of the examination it is as well to have before one plates on which the points of emergence of the principal sensory nerves are marked in black. (Plates are given by the author.)

With the faradic current, each induction shock produces a short pricking sensation which, when the current is making and breaking quickly, becomes continuous, stinging, and throughout the nerve a distal sensation, at first of tingling, later of pricking. The intensity of this faradic sensation increases with the rapidity of the interruptions. With the galvanic current, in addition to the distal sensation of pricking, is observed a keen sensation of burning of the skin, limited to the surface of contact of the electrode.

As is seen with the motor nerve, the cathode produces in the sensory nerve a reaction on closure and the anode on opening: the special quality of the cathode is much more intense. This is what Erb has called 'the law of the sensory shock'.

Normally the sensations developed by the electric current are manifested as much at the cutaneous surface immediately covered by the electrode as in the zone of distribution of the cutaneous nerve. In lesions of the nerve-trunk, even slight, one observes a limitation at the surface of contact of the electrode and an abolition of the radiation of the sensation in the sensory area of the nerve.

III. **Comparative examination between the electrical sensibility of the nerve-terminations and the conductivity of the electric wave across the sensory nerve.** In lesions of the nerve-trunks comparison of the fibres and the nerve-terminations can give the most dissimilar results. In slight lesions the following is most often seen: inexcitability of the afferent paths, hypo-excitability and occasionally hyperexcitability of the sensory terminations. Neri quotes some examples: A soldier complained of pain along the ulnar side of the left forearm and the two median digits. All the signs were negative, one only was positive: the inexcitability of the cutaneous branch of the ulnar nerve at the ulnar side of the wrist to which was added faradic and galvanic hypaesthesia of the two median digits. Such a finding justified the diagnosis of inflammation of the afferent roots of the eighth cervical and first dorsal nerves. Another example is one of sciatica, in which electrical examination of the sensibility gave exact proof and removed all doubts. The cutaneous sensory organs can react towards the electric current in an absolutely different manner to the afferent fibres.

In severe lesions hypo-excitability of the afferent paths and inexcitability of the sensory organs are noted. The inexcitability of the afferent paths and of the sensory organs indicates a syndrome of complete interruption which, ascertained long after the trauma, proves an irreparable lesion. In central lesions a parallelism between the results of the examination of the afferent paths and the sensory organs is always ascertained. One sees the medico-legal importance of electrical examination of the cutaneous sensibility which ought to take a great place in the semeiology of the nervous system.

P. L.-B.

## *Electrotherapy.*

**Delherm** et **Laquerrière**. L'électroradiologie dans les névrites motrices. [**Electroradiology in neuritis of motor nerves.**] *J. de radiol. et d'électrol.*, 1921, **5**, 97.

The authors show first of all that the contraction on electrical stimulation does not form the sole treatment in neuritis of a motor nerve, and, secondly, put forward the excito-motor method for each particular case and the manner of applying it.

I. **Applications without excito-motor action.** A. *Applications acting on tissues irritating or compressing the nerve.* (*a*) Radiotherapy often acts quickly and well; particularly in deep lesions, following pachymeningitis, contusion of the vertebrae, &c. It is equally useful in superficial cicatricial lesions. (*b*) In superficial scleroses and adherent cicatrices the constant current is the best form of treatment: the negative pole is placed over the spot where the nerve is caught up. If the cicatricial tissue has a greater resistance than surrounding tissue, most of the current passes through the latter. Sodium chloride and potassium iodide on the negative pole are the best salts to use.

B. *Applications acting on the nutrition, circulation, and trophic mechanism of the part affected.* The part as a whole and not only the injured muscle must be treated. (i) Coldness, circulatory disturbances, &c.: In preference to other methods stated, the authors use their thermo-luminous couple: an equally good procedure is friction with Oudin's electrode. In marked cases of coldness thermo-penetration can be used. (ii) Applications designed to act upon the trophic mechanism: If there be a total or partial R. D. the trophic action of the constant current alone must be used: if painful or spasmodic phenomena are present, muscular contraction should not be induced. The constant current can be applied in two ways: (*a*) Classical technique: the current is made to pass along the affected part; the authors recommend electrodes made of wet packs in preference to bath electrodes. The intensity varies according to the age of the patient, his build, the condition of the skin, &c.; the duration of the application is from 10–20 minutes. (*b*) Technique of Hirtz: the electrodes of wet packs, 3–4 cm. thick, are in the shape of long, broad bands; they are placed one on each side of the affected part. The intensity can be as high as 200–300 milliamps, and the duration 45–60 minutes.

II. **Applications producing an excito-motor action on the muscles.** When there is neither pain nor spasm, trophic applications should be associated with those designed to act on the muscle by making it contract. Muscles showing an R. D.: In severe lesions, trophic applications alone should be made at first, but later a few muscular contractions should be caused without fatigue. Sharp shocks from the constant current are generally used, but these make the neighbouring muscles contract or only cause a small amount of work on the part of the muscles which are really affected; also the amount of work done by the injured muscle cannot be gauged as is necessary. The authors, therefore, have recourse to the galvano-galvanization described by Babinski, Delherm, and Jarkowski. When the muscles are less injured the best excitant is an undulating galvanic current. When the muscles show a clear contraction and one not delayed, good exercise is obtained by the interrupted constant current.

When the state of degeneration in the various muscles is practically the same the whole limb can be acted upon: the electrodes for trophic applications are left in place, but a metronome is placed in the circuit. When, on the other hand, the muscles or groups of muscles are unequally affected, every muscle must work, and work at the degree which suits it. Four methods of bringing this about are given.

III. **Applications having an excito-motor action on non-degenerated muscles.** When a muscle only shows hyperexcitability it should be treated by the faradic current or one of that kind, but a tetanizing current must never be used. The induction shock is the simplest but, according to the authors, not the best, as it causes a brisk contraction. The tetanizing faradic current interrupted by the metronome causes a definite but short contraction; this is used in most cases. The undulating tetanizing faradic current causes effects closely allied to voluntary contraction. Electro-mechanotherapy with resistance consists in sending into a muscle an undulating current, while a resistance opposes the contraction: it is of great use in many cases.

IV. **Superadded neuropathic conditions.** Neuropathic conditions more or less severe and leading to impotence may develop in the course of any affection of long duration. The authors discuss these and their treatment.

V. **General guidance for treatment and conclusions.** The electrotherapeutics of motor-nerve neuritis are far from being of one kind: different procedures suit different cases. (1) In every case where possible (neuritis due to compression) the cause itself must be acted upon. (2) It is most useful to act upon the circulation of the injured part by different methods, of which the authors prefer light baths, thermo-penetration, and high-frequency friction. (3) It is essential to stimulate the nutrition of the affected parts by the constant current; this appears to the authors to be the basis of treatment in all cases of motor-nerve neuritis. (4) Treatment by excito-motor action will be chosen after the electrical examination. (5) Excito-motor applications will be made such that each muscle will contract. (6) As the case progresses the time given to muscular contractions is increased and that of the constant current decreased until it is omitted entirely. (7) When there is no R. D. the circulation and local nutrition can be attended to, best of all, by way of faradism. (8) Faradism can be employed in various ways, the most satisfactory being an undulating tetanizing faradic current. (9) The possibility of superadded neuropathic conditions must not be forgotten. P. L.-B.

**Chartier.** Traitement des reliquats médullaires et radiculaires de l'encéphalo-myélite épidémique. [**Treatment of medullary and radical after-effects of epidemic encephalo-myelitis.**] *Bull. offic. Soc. franç. d'électrothérap. et de radiol.*, 1920, Nov., 180. (*J. de radiol. et d'électrol.*, 1921, 5, 142.)

Epidemic encephalo-myelitis (lethargic encephalitis) leaves encephalic after-effects, among which is a pseudo-parkinsonian syndrome which may be noticeably improved by thermo-luminous baths followed by warm hydrotherapy and by static baths. But the author insists especially on medullary or meningo-radical after-effects; he has treated four cases and reports the most typical observation: a man of 50 taken with febrile malaise, considered at first to be rheumatism complicated by neurasthenia, headache, asthenia, stiffness of the neck, invincible diurnal sleepiness, nocturnal insomnia, difficulty of speech and of ocular accommodation. When the author saw him in June 1920 the encephalic phenomena were very few, but the medullo-radical manifestations became progressively accentuated: stiffness of the whole spine, permanent contraction in flexion, clonic movements, exaggerated reflexes, muscular atrophy, very sharp pains in the left upper limb; pains, also sharp, but less marked, and contraction in the superior right limb; spasmodic paresis with exaggeration of the reflexes in the lower limbs, &c. The treatment consisted of general thermo-luminous baths one day, localized on the spine, and followed by warm hydrotherapy the next day, and daily applications of high frequency on the spine and the painful plexus. First, development was arrested, and at the end of a fortnight an improvement which continued and increased. After five weeks treatment was continued by Dr. Menuet (Tours), who added cervico-dorsal radiotherapy. Three months after the beginning of treatment, and five months after the beginning of the disease, the patient was cured. Now, in the numerous similar observations which have been published and in which mention is never made of physical treatment, development towards cure is much more slow. In another case, the continuous current used to combat the muscular atrophy brought back the pains; it is therefore necessary to take care, and particularly to see that the current does not traverse the plexus and the spinal cord (for example, give the applications from the hand to the shoulder and not from one hand to the other). S. U. L.-B.

# MEDICAL SCIENCE

## ABSTRACTS & REVIEWS

VOLUME IV. NUMBER 6 SEPTEMBER 1921

## CONTENTS

REVIEWS: PAGE

DIABETES MELLITUS . . . . . . . . . . . . . 497
DISEASES OF THE PANCREAS . . . . . . . . . . 509
SPINAL, REGIONAL, AND LOCAL ANAESTHESIA . . . . . . 516
GRAFTS OF DEAD TENDON . . . . . . . . . . . 527
THE ELECTROMYOGRAM IN NERVOUS DISEASES . . . . . 530
THE EXPERIMENTAL PRODUCTION OF ALTERATIONS IN BRAIN VOLUME . . . . . . . . . . . . . . 535
THE BIOCHEMISTRY OF ECLAMPSIA . . . . . . . . . 537

ABSTRACTS:

NEUROLOGY . . . . . . . . . . . . . . 547
PATHOLOGY AND BACTERIOLOGY . . . . . . . . . 550
BIOCHEMISTRY . . . . . . . . . . . . . 573
RADIOLOGY AND ELECTROLOGY . . . . . . . . . 581

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*In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.*

# REVIEWS

## DIABETES MELLITUS

**Aetiology.** Castronuovo, of the Naples University Medical Clinic, maintains that among the causes and contributory factors of diabetes special importance should be attached to the immediate and late effects of infectious disease, especially the latent forms of malaria, tuberculosis, and syphilis. He considers that the large number of diabetic subjects in southern Italy is due not only to the diet but also to infective agents, especially malaria and tuberculosis, which produce changes in the digestive organs, nerves, glands of internal secretion, liver, and pancreas. In many cases of diabetes associated with tuberculosis the latter, far from being a late effect of the glycosuria, precedes it and favours its appearance, and then develops as an apparently new disease which runs a rapid course.

In a review of the literature relating to the association of glycosuria with infectious disease, Stengel, of the University of Pennsylvania, shows that with few exceptions the cases recorded were instances of temporary glycosuria accompanying the infection in question and probably occurring only during the febrile period. In only a few of the cases was the development of a permanent diabetes established. In a series of slightly over 200 cases of diabetes Stengel had eight post-infective cases, in which the patient was under observation long enough to determine that there was an actual diabetes and not a transient glycosuria. In 3 cases the infection was influenza, in 2 erysipelas, while scarlet fever, pneumonia, and vaccinia were responsible for one case each. In 5 cases it was certain that diabetes was not present before the occurrence of the infection, and in 3 the infection caused a relapse of an apparently cured diabetes. Stengel suggests that the diabetes in these cases was caused by pancreatic lesions contracted during the infection.

Diez, lecturer in surgical pathology in the University of Rome, has collected the following statistics showing the frequency of trauma preceding diabetes; in 20 out of 225 cases (Griesinger); in 2 per cent. out of 4,068 cases (Frerichs); in 1·4 per cent. out of 938 cases (Seeger); in 5 per cent. out of 116 cases (Ebstein); in 1 per cent. out of 800 cases (Senator); in 5·6 per cent. out of 669 cases (Külz-Rumpf). According to Lépine, trauma is a cause in 5 per cent. of all cases of diabetes, but not an exclusive cause, as in many cases there is a hereditary predisposition. Cantani found in 10 per cent. out of 1,004 cases of diabetes a history of trauma, but, as Ferranini observes, he included cases in which diabetes had developed 50 years after the trauma. According to Brouardel and Richardière traumatic diabetes is commoner in men than in women, while Lépine considers children as most likely to be affected. Diez, however, thinks that these statistics have only a relative value, because the writers had not made a sufficiently careful inquiry into the traumatic aetiology. Although all writers admit the existence of a traumatic transient glycosuria, some, like Jaccoud, deny the existence of a true traumatic diabetes and consider that trauma merely rouses pre-existing diabetes into activity. Others believe in the possibility of traumatic diabetes developing when a hereditary or acquired predisposition is present. The region on which the injury is inflicted is of importance. In 33 cases, Brouardel found cranial trauma in 17, spinal trauma in 5, and injuries of other parts of the body in 11. In 49 cases collected by De Sandro cranial trauma occurred in 27, spinal trauma in 12, and general or abdominal trauma in 10. The importance of cranial trauma is generally admitted. The injury is always severe, being sometimes accompanied by fracture and in most cases by concussion; in some cases, however, no appreciable damage to the nervous system has been detected. Spinal trauma may be of various kinds, such as a fall on the cervical, dorsal, or lumbar region. Sometimes there is fracture and dislocation, while in others there is no surgical lesion but only spinal concussion, especially in falls from a height. According to Brouardel and Richardière peripheral trauma of any kind is sufficient to cause traumatic diabetes, and it is not necessary that the part injured should correspond to a region in which the nerve centres are situated. Traumatic diabetes often appears early—that is, within the first few days, but sometimes there is an incubation period of several weeks, and in rare cases of from two to sixteen months. It is generally held that if diabetes occurs two years after the injury it has no relation to the trauma. The onset may be acute, and the subsequent course rapid or slow, or it may be insidious and progressive from the start. The symptoms of traumatic diabetes are the same as in spontaneous diabetes. Brouardel and Richardière, however, have emphasized the frequency of nervous symptoms, such as drowsiness, insomnia, psychical disturbance, delirium, headache, vertigo, and disorders of the special senses.

According to Joslin, who asserts that there are probably more than half a million diabetics in the United States, the statistics for the last thirty years show so great an increase in the number of diabetic patients that if it were not in part explained by a better recognition of the disease, the outlook for the future would be startling. In 1900 the death-rate from diabetes in the registration area of the United States was 10 per 100,000 and in 1915 18 per 100,000. In the same period it rose in Boston from 14 to 26 on the same basis.

Brigham states that from 1914 to 1920 628 cases of diabetes were admitted to the Massachusetts General Hospital, and the death-rate fell from 28 per cent. in 1913 to 5 per cent. in 1919, coinciding with the newer methods of treatment. In private practice the mortality was lower still, being only 2 per cent. in an even larger series of cases.

**Symptomatology.** Widal, Abrami, and Iancovesco, describe a new sign which consists in the fact that if a certain amount of glucose be given by the mouth to a true glycosuric his white blood count will shortly drop well below normal figures, then rise above normal, and drop to the ordinary count again—all within two hours.

This sign has been elicited with varying amounts of glucose and the minimal necessary dose seems not to exceed ten grammes. It is less easily evoked by other sugars. It does not vary with the amount of hyperglycaemia or glycosuria or acetonuria. It may be present when glycosuria is absent, provided the patient is a true diabetic. On the other hand it is not found in glycosuria of the renal type, i. e. due to an abnormally low renal threshold for sugar but unaccompanied by any hyperglycaemia.

It is not suggested that the sugar administered acts as a direct provoker of the haemoclasic crisis, but rather that it excites the action or formation of some unknown ferment or other body capable of so doing. For several reasons the authors are inclined to think that the primary action is one on hepatic metabolism.

Rathery and Binet made a study of the *saliva* in diabetic patients and found that it was diminished in amount, was frequently viscous, fairly frequently acid, and in some cases contained glucose in considerable proportions. Experiments on dogs whose blood-sugar had been increased by intravenous injection of glucose or removal of the pancreas showed that sugar was eliminated by the salivary glands. Cases have been recorded of glucosialorrhoea associated with glycosuria, alternating with it or occurring as an isolated phenomenon.

According to Kahn comparatively little attention has been given to the cardio-vascular changes present in diabetes, *angina pectoris* especially being overlooked. Unless granular changes in the kidney are present, the diabetic patient has usually a normal or low blood-pressure. Attacks of angina pectoris may nevertheless be the chief complaint of a middle-aged diabetic patient. Although the pain may not be very severe, it may still cause considerable anxiety. A remarkable feature of the attacks is that they do not occur when the patient's sugar tolerance is not exceeded. A high blood-sugar with glycosuria will frequently cause a recurrence of the attack. Electrocardiograms in such cases show an inversion of the T-wave in one or more of the three leads, which is usually due to some pathological condition of the myocardium. Kahn suggests that the myocardial lesions result from a lowering of the glycogen storage in the fibres of the bundle of His, which are normally richer in glycogen than the ordinary cardiac fibres. Of three cases of diabetes reported by Kahn two had a low blood-pressure and attacks of angina pectoris, while in the third high blood-pressure and albuminuria were present, but there was no complaint of any cardiac oppression.

According to Labbé, who records four cases, *diabetic epilepsy* is a rare condition which is associated not with hyperglycaemia but with acidosis. The convulsions occur in the course of severe diabetes, which is almost invariably accompanied by acidosis, either before or after the onset of coma. In some cases uraemic intoxication has been rightly held responsible, for a fair number of diabetics are also subjects of Bright's disease and die from uraemic coma.

Guillain reports a case in a soldier, aged 35, of epileptic convulsions occurring in the course of subacute diabetes with acetonuria. A left hemiplegia was present at the same time as the convulsions and disappeared with them, being doubtless due to a transient intoxication of the cortex.

From a study of 300 diabetic patients at the Mayo Clinic Wagener and Wilder found that *retinitis*, of which there were 80 cases, did not occur in uncomplicated cases of acute diabetes, but was present only in cases complicated by vascular or renal disease, in which the diabetes tended to be mild and chronic. They conclude that the primary cause of the retinitis of diabetes lies in the accompanying pathological changes in the vascular system, the more essentially metabolic disturbances of the diseases playing at most a secondary part.

Coutela, on the other hand, is opposed to the view that every case of retinitis in a diabetic patient is an albuminuric retinitis, on the ground that the existence of retinitis in diabetes without albuminuria, hypertension or azotaemia has been repeatedly demonstrated. The optic disk, which escapes in diabetes, is affected in albuminuria, so that in the former there is a pure retinitis and in the latter a neuro-retinitis. Moreover, the prognosis is different in the two cases. In albuminuric retinitis the prognosis as regards life is worse than in diabetic retinitis, whereas the prognosis as regards vision is much worse in diabetic retinitis. Blind albuminuric patients are rare, as they die before blindness occurs, whereas in diabetic retinitis blindness takes place long before death. This blindness is due to multiple causes, such as subintrant haemorrhage, haemorrhagic glaucoma, and separation of the retina. Although real differences exist between diabetic and albuminuric retinitis, Coutela points out that it is none the less true that the two affections are connected and that their coincidence is frequent and indeed the rule after a certain time.

Prym, who records a case of diabetes mellitus in a patient aged 20, accompanied by an extensive eruption of flea-bites, remarks that diabetics are especially liable to be attacked by fleas, owing to the fondness of these insects for sweet blood, and suggests that the cases of peculiar eruption in infantile diabetes reported by Bihlmeyer and Koch were examples of this kind.

As Fitz (1) points out, the assertion that diabetes is by no means exclusively a medical disease is proved by the fact that 54 or 14 per cent. of 386 diabetics admitted to the Massachusetts General Hospital from 1913 to 1917 inclusive presented *surgical complications*. Of the 45 cases who came to operation 20 were suffering from acute infection or gangrene, and 25 were non-infected cases. The mortality among the former was 50 per cent., and among the latter 12 per cent. Fitz emphasizes the importance of a course of diabetic treatment in preparation for operation when possible, especially in uninfected cases where the surgical complication is not an acute emergency. He regards local anaesthesia as safest for minor operations and gas-oxygen as best for major operations. Spinal anaesthesia may prove dangerous, and ether is contra-indicated on account of its pharmacological properties (cf. *Medical Science*, 1919, **1**, 279–81).

**Diabetes and tuberculosis.** The rarity of diabetes developing in patients with active tuberculous disease is shown by Montgomery's statistics, which are quoted by Janney and Newell. Among 31,834 cases of tuberculosis in 25 sanatoria in the United States there were only 101 cases with glycosuria, and only $\frac{1}{6}$ per cent. with diabetic symptoms, whereas more than 1 per cent. of the population develop diabetes. It is therefore evident that diabetes attacks the subjects of active tuberculosis less frequently than normal individuals. With regard to the frequency of tuberculosis among diabetics, while the older statistics reported an ncidence varying from 15 to 25 per cent., Joslin, in a series of 1,146 cases observed from 1894 till December 1916, noted only 3·1 per cent. as tuberculous. According to Janney and Newell all grades of diabetes may be found among glycosuric patients developing tuberculosis. In their series of 16 cases showing this association the diabetes was mild in 9, moderate in 4, and severe in 3. From a study of their cases they conclude that the untreated diabetic is more likely to develop pulmonary tuberculosis than when he is maintained sugar-free by modern diabetic methods. Of their 16 cases 12 definitely improved during a course of institution treatment, diabetic symptoms disappeared in all but 2 cases, and tuberculous symptoms improved in the majority of cases.

**Diabetes and leukaemia.** Fitz (2) records an example of the association of diabetes mellitus and myelogenous leukaemia in the same individual, of which only two previous instances have been recorded, namely, by Rebitzer in 1892 and by Schwarz in 1905. In Fitz's case the attack of diabetes was mild and responded to diabetic treatment, but was not appreciably influenced by X-ray exposure of the splenic region, which had a markedly beneficial effect upon the leukaemia.

**Diabetes and pregnancy.** According to Umber both internists and gynaecologists are agreed that it is very exceptional for diabetic women to become pregnant. Thus Naunyn, in his large experience, has seen only one case of severe diabetes with acidosis in pregnancy. Bouchardat, in his work on diabetes, states that he cannot remember having seen any pregnant diabetics, and von Noorden states that of 240 married women with diabetes only 9 became pregnant. Offenfeld in 1908 could find only 64 cases in the literature of diabetes in pregnancy. Most of the recorded cases were only mild forms of diabetes or transient glycosuria. Hitherto no case of diabetic coma during pregnancy has been reported, and it is relatively rare for a diabetic patient to die directly after delivery. Umber, however, has seen three cases in which death from diabetic coma occurred during pregnancy. In two of the cases acidosis had preceded pregnancy, showing that diabetes is no obstacle to conception. In the third case Caesarean section was performed during coma in the seventh month of pregnancy, but neither mother nor child could be saved. Although artificial interruption of pregnancy was not of any benefit in this case, Umber recommends that pregnancy in diabetics should be interrupted as early as possible, even in cases without acidosis, if before pregnancy menstruation has been found to exert an unfavourable influence in diabetes.

Andérodias and Dubreuil state that the association of glycosuria and pregnancy may take place under two different conditions. (1) A woman with diabetes may become pregnant. (2) A woman who has hitherto been healthy may develop glycosuria in the course of one or several pregnancies. Both these occurrences are rare, the writers having seen only two examples in the last twenty years. In the first case a diabetic patient whose urine contained 20 to 40 gm. sugar per litre of urine gave birth to a full-term macerated foetus weighing seven kilos, which had died *in utero* eight days before birth. In the second case the woman had had glycosuria during her last two pregnancies but with no other signs of diabetes, and the urine between these pregnancies had been normal. Examination of the urine during the following pregnancy showed an amount of sugar ranging from 50·75 gm. to 52 gm. per litre. A still-born child weighing 5½ kilos was born at the end of the eighth month, and examination of its pancreas showed enormous enlargement of the islands of Langerhans, the function of which is to control the sugar content of the blood.

In a study of 2,200 consecutive cases at the Obstetric Department of the University Hospital, Ann Arbor, where the patients' urine is examined at least once every week, Cron found that 88 or 4 per cent. gave a test for some form of sugar during pregnancy, labour, or the puerperium, the incidence being as follows: pregnancy 68 or 77 per cent.; puerperium 14 or 15 per cent.; pregnancy and puerperium 6 or 7 per cent. Cron points out that a positive reaction during pregnancy does not necessarily indicate the existence of diabetes mellitus, but is usually due to lactosuria or alimentary glycosuria and rarely to renal diabetes. Lactosuria is common during pregnancy and the puerperium. It is entirely physiological and must be differentiated from the various types of glycosuria. Cron estimates that 30–50 per cent. of pregnant women present alimentary glycosuria. They have no hyperglycaemia and are not true diabetics. The association of diabetes and albuminuria is an ominous complication, and in Cron's opinion calls for an immediate interruption of pregnancy.

**Diabetes and hirsuties.** Weil and Plichet have collected three cases reported by Guemes, Tuffier, and themselves respectively of glycosuria in women associated with hirsuties. In Guemes's case the glycosuria was only slight and transient, and in Tuffier's abundant and persistent, while in their own case there was a true diabetes accompanied by polydipsia, polyphagia, and loss of flesh, and complicated by fatal pulmonary tuberculosis. The writers point out that the association of diabetes mellitus with hirsuties is not a mere coincidence, and allude to the investigations of Laignel-Lavastine, who in two cases of hirsuties without glycosuria was able to detect a latent disturbance of metabolism which was shown by the appearance of glycosuria on subcutaneous injection of suprarenal extract, thyroid extract, or extract of the whole pituitary gland or of its posterior lobe only, whereas in a control glycosuria was produced only by injection of extract of the posterior lobe. The form of diabetes associated with hirsuties is similar to that found in other diseases of the endocrine glands, such as acromegaly or Graves's disease, in which affection of the hypophysis and thyroid involves the hepato-pancreatic system which controls the metabolism of starch.

**The blood-sugar in diabetes.** Pickering made observations on the blood-sugar in 50 cases of diabetes, and came to the following conclusion: (1) The blood-sugar is almost invariably raised in diabetes. (2) It tends to increase with the duration of the disease. (3) It varies directly with the clinical severity, but in mild cases with albuminuria or a history of heavy consumption of alcohol or tobacco it is often high. (4) It is reduced by fasting. (5) The reaction of blood-sugar to dietetic treatment is of more importance than its height. (6) A blood-sugar persistently above normal in spite of treatment is not invariably a bad sign, for the blood-sugar does not always fall to normal when the urine is kept sugar-free for a long time. (7) The blood-sugar corresponds more closely with the carbohydrates in the food in mild cases and with the glycosuria in severe cases. (8) The amount of carbohydrate in a meal taken from 1¼ to 2 hours beforehand appears to have no effect on the blood-sugar. Apart from fasting or very low diet, the amount of food, other than carbohydrate, taken on the previous day frequently had little or no effect on the blood-sugar. (9) A high renal threshold did not appear to be a bad sign. (10) A study of the blood-sugar, particularly of its variations under treatment, is of great value in forming an opinion of the nature and probable course of a case.

**Renal diabetes.** Paullin states that the essentials as agreed on by the majority of writers for the diagnosis of renal glycosuria are as follows: (1) A normal blood-sugar content of between 70 and 110 mgm. per 100 c.cm. of blood. (2) The constant presence in the urine of sugar which is definitely known to be glucose. (3) Little if any change in the glycosuria or increase or decrease in the carbohydrate content of the diet. (4) An absence of the usual symptoms of diabetes mellitus, such as polyuria, polydipsia, polyphagia, and loss of weight. Although the condition is not common Paullin thinks that there are probably many more patients under treatment for mild diabetes who have really renal glycosuria than our present knowledge would indicate. A similar view is held by Galambos, assistant at the Buda Pesth University Medical Clinic, who states that though barely two dozen cases of renal glycosuria have been recorded, he has seen two cases within a few months. He therefore concludes that it is not the occurrence but rather the recognition of the condition which is so rare. He points out that different views are held as to the relation of renal glycosuria, or of its chronic form renal diabetes, to diabetes mellitus. While von Noorden does not recognize the independent existence of renal diabetes, G. Klemperer and numerous other investigators regard renal diabetes as a mild disease of the kidneys with an abnormally increased permeability for sugar, and therefore not as an essentially metabolic disorder.

Strouse records four cases of renal glycosuria, two of which had been under observation for two years, one for almost five years, and one for eight years. All four showed glycosuria and none symptoms of diabetes mellitus. In one case tests for renal function seven years after the onset showed no depression of renal function except as regards phthalein excretion.

**Prophylaxis.** Williamson has drawn up the following recommendations based on what is known of the aetiology of diabetes with a view to postponing the onset of the disease or possibly preventing it. (1) All persons, even those who are in good health, should avoid great excess of sugar, jam, sweets, chocolates, sweet foods, and sweet drinks. (2) If through a family history of diabetes, race tendency to the disease, or on other grounds the onset of diabetes is feared, but sugar has never been found in the urine, the following precautions are advisable: (*a*) The amount of sugar in the diet should be restricted. (*b*) Excess of alcohol should be carefully avoided, especially excess of beer and alcoholic beverages containing much sugar, e.g. port, tokay, and champagne. (*c*) Excess of food should be avoided, as this is probably a predisposing cause in some cases. If very large quantities of food have been taken, and difficulty is experienced in restricting the amount, foods like green vegetables and jelly, which contain little absorbable foodstuff in the large bulk consumed, should be taken freely. (*d*) A tendency to obesity should be checked, since the mild form of diabetes is often preceded by obesity. (*e*) Sufficient physical exercise is very important. (*f*) Excessive brain-work and severe brain-strain should be avoided. (3) If sugar has been found in the urine once, and has then disappeared, it is desirable to determine if the power of sugar destruction is diminished. (4) If the glycosuria is temporary but the power of sugar destruction is diminished, all sugar and all food or drink containing sugar should be cut off from the diet, and the amount of starchy carbohydrates should be reduced. (5) If the glycosuria is intermittent or permanent but slight, treatment suitable for a mild diabetes should be followed.

Joslin, who found that marked obesity preceded the outbreak of the disease in more than 40 per cent. of his 1,063 cases of diabetes, points out that the preponderating influence of obesity in the development of diabetes explains various peculiarities in diabetic case histories, such as conjugal diabetes, the frequency of the disease in Jews, the richer classes of society, and mental workers in contradistinction to physical workers, and its occurrence as an sequel of infectious diseases. Joslin therefore urges that obese patients should be frankly told that they are candidates for diabetes. Brigham also asserts that the prevention of obesity will reduce the number of diabetics tremendously, and Stark, who regards prophylaxis as important as therapeutics in combating diabetes, maintains that obese and gouty persons as well as those who eat too much should ever be watchful of the disease. Joslin states that it is rare for diabetes to develop in an individual above the age of 20 who is habitually under weight, and when it does so develop the case will usually be found to be either extremely severe, extremely mild, or associated with a marked hereditary taint or degenerative stigmata. He also makes a plea for early diagnosis, as, if the disease is detected early, it is far more susceptible to diet. He urges that the custom of urinary examinations should be made more frequently and more universally and suggests that every one should have the urine examined on his or her birthday. Lauritzen, of Copenhagen, also recommends that in families in which diabetes occurs the doctor should occasionally test the children for glycosuria, particularly after acute febrile illnesses, in furunculosis, or in case of other symptoms indicative of hyperglycaemia, eventually prescribing a starchy meal and examining the urine passed after the lapse of four hours. In diabetic families the doctor should direct the parents to avoid giving the children a diet too rich in carbohydrates. In life insurance examinations, in polyclinics, and in hospitals, when a reduction is found in the patient's urine, an examination after a test meal should be made in doubtful cases. Diabetes may thus often be discovered in its incipient stages (*vide* also *Medical Science* 1920, **2**, 315).

**Treatment.** A.—General. Janney states that in the Santa Barbara Memorial Metabolic Clinic, an institution specially organized for the study and treatment of metabolic diseases, a class has been formed in which diabetic patients are given instruction as to the dangers of their disease, the peculiarities of individual reaction to it, diabetic dietetics, laboratory tests, and what to do in emergencies. The subjects include the normal chemical processes of the body, diabetic chemical processes, fasting and low diabetic diet, medium and high diabetic diets, chemical demonstration of the simpler tests necessary for diabetic treatment, and a discussion of acidosis. The patients are said by Janney to show astonishing eagerness to benefit by the instruction, and the fact that increasing numbers of diabetic patients are contriving to live sugar-free for indefinite periods after a course of treatment in the clinic is attributed in large measure to systematized instruction.

Allen and Wishart, whose previous researches on the relation between hyperglycaemia and glycosuria in pancreatic diabetes have been described (vide *Medical Science*, 1920, **3**, 278), report further experiments on dogs which show that (*a*) the increased metabolism of exercise does not impose an added strain upon the internal pancreatic function; (*b*) the combustion of food materials through the increased muscular metabolism and mass resulting from exercise is a definite relief compared with the accumulation of such materials through inactivity; (*c*) the internal pancreatic secretion is nevertheless an indispensable intermediary in such combustion, and exercise merely enables the muscles to make use of such quantity of this secretion as is available to them, but cannot compensate when this quantity falls below the necessary minimum. Allen and Wishart point out that, though the combustion of food by exercise is preferable to its deposit in the body, exercise cannot replace restriction of diet or permanently atone for excessive diet. The fundamental value of exercise is probably as a form of undernutrition. The combustion of calories by exercise, however, is not so beneficial as removing them from the diet and loses its potency at a stage when dietetic undernutrition is still effective. Impairment of sugar utilization by exercise occurs only in the extreme stage of diabetes, but in human patients the nervous and systemic influences must also be considered. With any important degree of undernutrition heavy exercise involves undesirable fatigue and strain, but light exercise aids health. Rest is necessary in the severest cases. The writers conclude by saying that the modern dietetic treatment of diabetes differs in two principal respects from former practice: on the one hand heavy exercise formerly advocated for burning up surplus sugar is discouraged, on the other hand the hygienic benefits of lighter exercise are made available to many patients to whom exercise was formerly forbidden.

B.—Dietetic treatment. If an ordinary diabetic diet with restriction of carbohydrates fails to check the glycosuria promptly, Williamson (2) recommends rest on the sofa for seven days, and a mixture of eggs, cream, and water, prepared as follows: 3 eggs are beaten up with 3 oz. of cream and a little water. More water is then added gradually until the mixture measures four pints. Half a pint of this mixture is taken two-hourly from 8 a.m. to 10 p.m. and in addition coffee or tea is given at 8 a.m. and 4 p.m. and also half a pint of beef tea at noon, 6 p.m., and 10 p.m. No other food is given during this period. In many cases the glycosuria is checked in from four to seven days. The diet is then slowly changed to a solid diet containing only a small amount of carbohydrate food. It is often found that not only has the glycosuria been temporarily arrested by this regimen, but that the power of carbohydrate destruction in the system has been increased, so that the patient can take for a short or long period an amount of carbohydrate which would have been attended with glycosuria before the treatment. This diet is contra-indicated in cases with marked acidosis or with certain complications, such as phthisis and marked wasting or cardiac failure.

According to Allen the following five facts may serve in planning diets after fasting: (*a*) the total calories at first should be very low and increased gradually; (*b*) protein is the most important food; (*c*) the tolerance for protein is highest when other foods are excluded or closely restricted; (*d*) the caloric requirement falls with the body weight and may reach a very low minimum; (*e*) the tolerance rises as the weight falls, and with exceedingly few exceptions the two curves intersect at some level at which life can be supported. Although in some elderly patients slight hyperglycaemia and nitroprusside reactions may be permissible to avoid undue hardships, Allen points out that diabetes after forty is by no means always benign and not infrequently requires stringent measures to control it, especially after long neglect. The more severe the diabetes and the younger the patient, the more vigorously should hyperglycaemia and all the other symptoms be controlled from the outset.

Mosenthal and Wiener, of the Department of Metabolism, Vanderbilt Clinic, New York City, remark that the measured diets in the modern treatment of diabetes must meet two requirements: (1) control of the glycosuria and (2) control of the acidosis. The first of these is effected by regulating the consumption of the carbohydrates and the second by adjusting the fat intake. In view of the fact that curtailment of the fatty foods will prevent or postpone acidosis and coma, two sets of diets are necessary, viz. (1) in which the fats are reduced to a minimum (minimal fat diet), and (2) in which fats are allowed more liberally but in limited amounts (low fat diet).

The writers have drawn up tables showing details of these minimal fat and low fat diets, in both of which the only carbohydrate is contained in green vegetables.

From experience of the method in 73 diabetic patients, Newburgh and Marsh are convinced that a high fat, low protein, and low carbohydrate diet is the only one which will keep the diabetic sugar-free, prevent the occurrence of serious acidosis, maintain nitrogen balance, and make it possible for the patient to resume the ordinary activities of life.

Allen, Mitchell, and Sherrill, who report three cases of combined diabetes and nephritis, state that the treatment of such cases is conducted according to the usual principles of the two diseases. Diabetic treatment by means of a high protein diet, gluten bread and the like may be inimical to an associated nephritis with impaired nitrogen excretion, but it is easily possible to adjust the protein ration to both diseases. If meat is forbidden in the treatment of hypertension, the diet of a diabetic with hypertension is seriously limited, but with restriction of salt such a patient is able to choose his own protein at will. One of the greatest dangers formerly consisted in acidosis in conjunction with nephritis, but this is avoided by treatment which keeps acidosis strictly absent.

Lauritzen states that diabetic therapy has been tending more and more towards individualizing dietary treatment owing to the diversity of the disease, of which mild, moderate, and severe forms are found. He recommends that each patient should be carefully examined and given the diet that qualitatively and quantitatively suits him at the time. Details are given as to the diet for recent uncomplicated cases, whether mild or severe, incipient diabetic coma, and diabetes complicated by other diseases.

According to Reimer, of the Heidelberg University Medical Clinic, the administration of *caramel* as a carbohydrate cure, introduced by Grafe, deserves more general recognition owing to its high calorie content and its simultaneous action in promoting elimination of sugar and preventing acidosis. The only contra-indication to its prolonged administration is severe diarrhoea. From his experience of the treatment in 55 patients, 19 of whom were aged from 14 to 34, and 36 from 36 to 64, Reimer found that it was most effective in cases under 34. A moderate degree of water retention was several times observed, especially when alkalis were administered simultaneously. Oedema due to caramel only was rare. In a few cases a slight increase in glycosuria was detected, but in no case was it of long duration. The best form of administration was 100 to 200 gm., in coffee, pudding, or alcohol, several times a day, with an equal quantity of fat in the food and a small amount of vegetables. Care should be taken not to give large amounts of carbohydrate, especially potatoes, at the same time as the caramel, or to add albumin to the diet, especially in the form of meat.

C.—Drugs. The use of *sodium lactate* in large doses in diabetes is recommended by Curatolo, who claims that it diminishes the polyuria, neutralizes the acidosis, and considerably reduces the glycosuria. Of all alkaline drugs sodium lactate is to be preferred, as it can be tolerated in large doses from the onset of diabetes. It can be given in combination with bicarbonate and citrate of soda. If sodium lactate is not available, equal parts of lactic acid and sodium bicarbonate in watery solution can be prescribed.

A case of diabetes mellitus successfully treated by *novarsenobenzol* is reported by Porter, of Bombay, who states that a practitioner with a large native practice in Bombay had treated over 50 cases of diabetes and glycosuria by intravenous injections of '606' without any relapses.

Vigevani, of Milan, states that under *pituitary opotherapy* the total quantity of urine in the twenty-four hours showed a considerable diminution in all diabetic patients with pronounced polyuria, and in those in whom the polyuria was relatively slight there was also a fall in diuresis to below normal. The duration of the antidiuretic effect in any case was limited to the period during which the pituitary substance was given and disappeared more or less completely afterwards. The antidiuretic effect of preparations of the whole gland was more marked when given by the mouth than when injected subcutaneously. Preparations of the posterior lobe only, when given subcutaneously, were less active still in the majority of cases. The dose of pituitary preparations required to obtain the greatest antidiuretic effect was not the same for all the patients and varied from 30–49 cgm. of the fresh gland in the twenty-four hours. When larger doses were given, the antidiuretic action diminished more or less considerably, without there being any appreciable change in the blood-pressure.

On the other hand, as the result of numerous investigations, Schenk, of the Breslau University Medical Clinic, found that pituitary extracts which in normal persons and in patients with diabetes insipidus give rise to transient anuria, in cases of diabetes mellitus either had no effect at all or diminished diuresis in only a slight degree. Increase of diuresis was never observed. The diuretic effect of the sugar in the diabetic patient is therefore stronger than even the extraordinarily powerful action of large doses of pituitary extract.

Laura, of New York, reports on the use of a serum obtained from a horse immunized with pituitrin in 30 cases of diabetes mellitus. Eight did not respond to treatment with any noteworthy diminution of glycosuria, 14 had a complete disappearance of sugar and increase of carbohydrate intake as well as a relief of symptoms, such as neuritis, retinitis, emaciation, headache, pruritus, polyuria, and polydipsia, and 8 had a diminution of glycosuria, or, to be more correct, an increased tolerance for sugar.

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## DISEASES OF THE PANCREAS

**Annular pancreas.** Benedetti reports an example of this rare anomaly, of which only six cases have been previously recorded, four having been discovered *post mortem* and two at an operation for intestinal obstruction. The present case occurred in a soldier who, while recovering from multiple gunshot wounds of the limbs, suddenly developed symptoms of intestinal obstruction. Death took place without operation, and at the autopsy the descending part of the duodenum was found to be constricted by a ring of pancreatic tissue. On naked-eye examination the pancreas appeared oedematous throughout, as if it were inflamed, but no microscopical examination was made. Benedetti states that Gianelli has recently shown that in teleostean fishes the pancreas usually surrounds the intestine, so that the annular pancreas in man may be regarded as an anomalous repetition of what is normally present in the lower vertebrates.

**Congenital steatorrhoea.** Miller and Perkins report a case of congenital steatorrhoea, only one previous instance of which, recorded by Garrod and Hurtley in 1913, has been published. In neither case was there any other evidence of pancreatic disease. The case described by Miller and Perkins was that of a boy aged 3 years, who had passed separated liquid fat since birth, and persisted in doing so except on a diet markedly low in fat content. In spite of the failure in absorption of fat there was no definite stunting of the child's stature by the age of 3 years. The writers adopt Garrod's suggestion of an inborn error of metabolism probably due to the absence of a normal enzyme, presumably a pancreatic enzyme, without any real disease of the pancreas.

**Necrosis of the pancreas.** According to Rohde, two principal varieties of pancreatic necrosis may be described: (1) primary necrosis which is caused by toxic, trophic or traumatic factors affecting the pancreas itself, with a relatively favourable prospect of cure by drugs or expectant treatment; (2) secondary necrosis caused by interference with the pancreatic blood-supply, in which case a cure is impossible without operation. Rohde reports a fatal case of secondary necrosis of the pancreas with considerable haemorrhagic effusion into the abdominal cavity, the necrosis being due to a sarcoma of the fundus of the stomach. Owing to the absence of severe gastro-intestinal disturbance the presence of a gastric tumour was not suspected until an exploratory operation was made. In spite of complete necrosis of the pancreas the urine was free from sugar until death. The absence of glycosuria in intra-abdominal haemorrhage for which there is no obvious cause does not therefore exclude disease of the pancreas, and Rohde recommends that if a large haematoma of uncertain origin is found in the course of an exploratory operation, the possibility should always be considered of pancreatic haemorrhage in man, and also in women if a ruptured tubal pregnancy can be excluded.

Mayer records a case of acute haemorrhagic pancreatitis with necrosis in a man aged 53, in whom rapid recovery took place after operation. The diagnosis was facilitated by the following considerations: (1) bulging of the epigastrium due to distension of the stomach accompanied by a board-like resistance of the epigastric portion of the rectus muscles: (2) infra-umbilical distension produced by distension of the transverse colon, which had been pushed downward. A bilocular condition of the abdomen had thus been produced; (3) the extreme intensity of the pain localized in the abdomen and radiating to the back and then throughout the abdomen; (4) the rapid occurrence of vomiting after the onset associated with normal action of the bowels excluded intestinal obstruction and perforative peritonitis; (5) the absence of fever, accompanied by a rapid pulse and signs of peritonitis differentiated the condition from acute cholecystitis; (6) the presence of blue spots which were observed at the umbilicus has been noted in other cases and was probably a trophic phenomenon due, like the pain, to irritation of the coeliac plexus; (7) the absence of glycosuria was not surprising, as the preservation of even a minute portion of pancreas is sufficient to prevent diabetes.

**Chronic pancreatitis.** Nicoll maintains that chronic pancreatitis is a more frequent occurrence than is generally supposed. Not only does it complicate catarrhal affections of the duodenum, biliary apparatus (whether the seat of cholelithiasis or not), vermiform appendix, and colon, but apparently it may exist as an independent affection. Owing to the difficulties in the diagnosis Nicoll has made it a routine procedure to resect a small wedge for microscopical examination in cases where there is any doubt as to the actual cause of the abdominal symptoms present.

In an article on the diagnosis and pathology of diseases of the pancreas, Gross, of the Greifswald Medical Clinic, confines himself to a consideration of the following diseases which specially interest the internist: (1) **Cirrhosis of the pancreas**, or, as Gross prefers to term it, **pancreatic sclerosis** or **induration**, is a condition analogous to cirrhosis of the liver, with which it is often associated. Vascular disease due to syphilis and arteriosclerosis, and congestion caused by alcohol or gall-stones are the most important aetiological factors. Gross maintains that this condition, at least in its milder forms, is more frequent than has hitherto been supposed, though he considers Kehr's estimate of having found it 69 times in 220 operations for gall-stones as exaggerated, the diagnosis in these cases having been based on: (i) Cammidge's reaction, and (ii) palpation during laparotomy, both of which tests Gross regards as fallacious. The symptoms, which are not characteristic, consist in loss of appetite, occasionally constipation, more frequently diarrhoea, and a feeling of weight in the epigastric region. The condition may last for years and subside when the causal factors are removed. Treatment must as far as possible be directed to removal of the cause, whether it be syphilis or gall-stones. (2) A much more severe form of pancreatitis, according to Gross, is **atrophy of the pancreas**, which is usually the consequence of chronic intoxications, such as lead-poisoning and especially alcoholism. The symptoms are very severe and the prognosis absolutely unfavourable. The patients suffer from vomiting, but the principal and most distressing symptom is a violent and extremely foetid diarrhoea, large masses of fat and undigested meat-fibres being present in the stools. The urine contains glucose, although usually severe diabetes is not present. Death from exhaustion occurs in one or two years. In addition to changes in the pancreas, which consist in loose soft connective tissue replacing the glandular substance and fine concretions in the ducts, the autopsy frequently shows lesions in the liver due to the same cause. The condition is distinct both from cirrhosis of the pancreas and from the atrophy of the organ which occurs in diabetes or in old age. (3) **Achylia** or **hypochylia pancreatica.** Gross states that this condition is not diagnosed in most cases, as it can only be identified by pancreatic tests. It is usually associated with gastric achylia or hypochylia. If a patient presents a deficiency of hydrochloric acid, and organic causes, especially gastric catarrh, can be excluded, and diarrhoea is present, the condition is probably one of pancreatic achylia as well as a gastric achylia. Examination of the stools always shows a deficiency of pancreatic juice, which is indicated by an extraordinary delay in the digestion of casein. The patients present the usual symptoms of achylia, especially diarrhoea, which is not affected by regulation of the diet, but the symptoms are never so violent as in organic disease of the pancreas. The condition is relatively harmless and is never fatal. Like gastric achylia, it is undoubtedly a purely functional disease. Treatment consists in administration of pancreatic ferment as well as hydrochloric acid and allowing the patient to eat anything apart from any very indigestible food.

**Syphilis of the pancreas.** Wile remarks that in spite of Neumann's statement in 1899 that the diagnosis has practically never been made during life or at least without operation, a number of cases are on record in which undoubted syphilis of the pancreas was diagnosed *intra vitam.* Although most authorities hold that the disease is exceedingly uncommon, Sallis, who collected 15 cases of syphilitic pancreatitis in 1913, asserts that the condition is not so very rare, and states that Warthin also holds that chronic interstitial pancreatitis is one of the most frequent visceral lesions found at necropsies in cases of latent visceral syphilis. Syphilis of the pancreas occurs in a sclerous and a gummatous form, and a combination of the two forms is also found. The symptoms of syphilitic pancreatitis differ but slightly from those of any other pancreatic disease, and the pancreas is so seldom attacked alone that the symptoms are frequently masked by those of involvement of the other viscera. The few points suggestive of syphilis when the pancreas is the seat of disease are jaundice without other cause, glycosuria and tumour of the pancreas without cachexia. The diagnosis is extremely difficult. Except for the predominance of glycosuria, which occurs in about 50 per cent. of the cases, and the relatively mild cachexia in association with a large palpable tumour, there are no definite criteria, according to Wile, to differentiate syphilis of the pancreas from cholelithiasis and from other forms of pancreatic disease, such as carcinoma or chronic pancreatitis. The association of hepatic disease, however, is strongly in favour of syphilis, and the therapeutic test is in most cases the most valuable guide. Although Neumann regards the prognosis as unfavourable, as most of the cases have only been recognized at the autopsy, Wile has collected 10 cases in which complete recovery was reported as the result of administration of salvarsan, mercury, or iodide, or of mercury and iodide combined.

Udaondo and Carulla report the case of a man aged 26, who for a year had presented symptoms of pancreatic insufficiency, viz. diarrhoea and pasty stools, which were refractory to ordinary treatment. He had never had any venereal disease, but examination of the patient and one of his brothers showed certain stigmata of hereditary syphilis. Mercurial treatment was adopted, with the result that the diarrhoea was rapidly cured and the general condition improved. The writers state that hereditary syphilis chiefly attacks the pancreas after the fifth month of intra-uterine life, and shortly after birth. Sclero-gummatous forms are the least frequent, and extra- and intralobar pancreatitis with hypoplasia of the glandular tissue has been found in almost all cases. No previous instance has been recorded of a patient who did not develop symptoms till adult life. In the present case the symptoms indicate functional insufficiency of the gland without obvious involvement of the internal secretion, as there was no glycosuria and no evidence of other glands of internal secretion being affected.

**Carcinoma of the pancreas.** According to Futcher, carcinoma of the pancreas, confirmed by autopsy or operation or both, occurred in 31 cases among the first 41,949 patients admitted to the medical wards of the Johns Hopkins Hospital. In 29 of these the disease was primary in the gland. Of the 31 cases, 22 were males and 9 females. The largest proportion—15—occurred in the fifth decade. Only one occurred in the coloured race. The important diagnostic signs were as follows: pain in 25, persistent and increasing jaundice in 23, palpable tumour in 12, distended gall-bladder in 21, emaciation and cachexia in 29, neutral fat and fatty acid crystals in the faeces in 17. Other interesting features were as follows: vomiting in 5, oedema of the feet and ankles in 5, ascites in 4, enlargement of the liver in 12, intermittent glycosuria in 3, acholic stools in 22. The treatment is practically hopeless and chiefly palliative. Pancreatic preparations may aid intestinal digestion and help to lessen the severe emaciation. Cholecyst-enterostomy or production of a biliary fistula is a possible means of relieving the intolerable pruritus due to the intense jaundice.

Speed has collected 52 cases of primary carcinoma of the pancreas from his private practice and the statistics of the County Hospital, Chicago, for the last six years. The average age at the time of diagnosis was 57, the youngest patient being 36 and the oldest 76. The most constant symptom was cachexia, which was present in 90 per cent., being apparently caused by the loss of fat in the stools. Jaundice was found in 80 per cent. Pain, usually of a cardialgic or gastralgic character, was present in 61 per cent. The discovery of an abdominal tumour by the patient or the doctor was made in 55 per cent. Ascites was present in approximately 20 per cent., as was also haemorrhage, which occurred in 11 patients, in 2 from the mouth, in 4 from the nose, in one from the bowel, in 2 from the buttocks and skin, and in 2 from the stomach. Oedema of the lower extremities occurred in 6 per cent. Steatorrhoea and azotorrhoea were not constant and did not occur till late. Speed maintains that there are no pathognomonic symptoms because the disease is too often overshadowed by symptoms of involvement of the neighbouring structures, such as the stomach, duodenum, bile-ducts, and colon. In the 11 cases which came to autopsy the head of the pancreas was most often involved by cancer, the body next, and the tail least often. None showed pancreatic calculi. Metastases usually first occurred in the lymphatic glands round the pancreas and bile-duct areas. The liver was the most often invaded of the neighbouring organs. 13 of the patients were operated on, mostly for gall-bladder drainage or removal.

Adams, who regards carcinoma of the pancreas as a relatively uncommon disease, states that only 8 cases have come to autopsy since 1913 at the Peter Bent Brigham Hospital, Boston. In 3 of these cases the head was involved primarily, in 1 case the head and body: in 3 cases the cancer was diffuse throughout the organ, and in 1 case it was limited to the tail; 2 carcinomas were of the scirrhous type, 5 were adenocarcinomas, and 1 was interpreted as having arisen from the islands of Langerhans. Extensive metastases occurred in 6 of the 8 cases. Adams emphasizes (1) the tendency of these tumours to invade the blood-stream locally; (2) the occurrence of generalized carcinomatosis by blood dissemination, and (3) the signs caused by secondary growths in two patients which obscured the clinical picture.

Adler, who reports a case of carcinoma of the pancreas with erosion into the transverse colon and lower part of the duodenum, is of opinion that ulceration of the abdominal viscera by pancreatic carcinoma is frequent. He has collected records of 11 histologically confirmed cases of primary carcinoma of the pancreas which came to autopsy from the wards of the University and Philadelphia General Hospital from 1876 to 1916. In 6 there was an ulcerating cavity leading from the tumour mass into one or more of the hollow viscera. In 4 the organ into which ulceration took place was the duodenum, in 4 the transverse colon, in 2 the stomach, and in 1 the gall-bladder.

**Pancreatic calculi.** Symes records a case of a man aged 40 who developed the characteristic stools of pancreatic insufficiency some months before symptoms of a calcium oxalate stone in the duct. The stone apparently ulcerated its way out of the duct into the bowel. Subsequently the symptoms and signs of pancreatic insufficiency became more marked, doubtless owing to cicatrization and gradual narrowing of the lumen of the duct and progressive fibrosis of the pancreas. Other points of interest in the case were (1) the rapid and ultimately fatal rise of blood-pressure due to auto-intoxication from the bowel or to imperfectly antagonized suprarenal secretion; (2) the long-continued good nutrition and physical and mental energy of the patient indicating to how great an extent pancreatic digestion may be assisted by other organs : (3) relief afforded to the patient by withdrawing fat from the diet and giving acid preparations by mouth after meals, the increased acidity stimulating the flow of secretion, and thus increasing both the internal and external secretions of the pancreas.

Apolloni records the case of a woman aged 20 who had suffered from diabetes for about a year and two or three months before death showed signs of tuberculosis in both lungs. At the autopsy, in addition to extensive pulmonary tuberculosis, the pancreas was found to contain a turbid fluid with calcareous sand, numerous small friable calculi and a large solitary calculus in the head of the organ inside the principal duct. Histological examination showed the presence of sclerotic glandular tissue with a few islands of Langerhans in a good state of preservation. The liver presented intense haemosiderotic pigmentation of the endothelium and Kupffer's cells, some of which were necrotic.

**Diagnosis.** Garrod remarks that Wardell's statement in 1871 that 'no symptoms are pathognomonic of pancreatic disease: an assemblage of symptoms indicates the probability of its lesion' still holds true to-day, though we have at our disposal a far greater assemblage of symptoms than Wardell had, and in not a few cases the degree of probability is not to be distinguished from certainty. Garrod classifies the diagnostic indications of disease of the pancreas into three main groups: (1) clinical signs and symptoms, such as tumour, pain, tenderness, vomiting, cyanosis, and signs of pressure on neighbouring structures ; (2) signs of failure of external secretion, defective digestion of proteins, fats, and carbohydrates ; (3) indications of failure of internal secretion, of which glycosuria is the most important and best known.

Wallis describes the various tests for the functional activity of the pancreas and comes to the following conclusions : (1) There is no one test so far devised which is pathognomonic of pancreatic insufficiency ; (2) the association of positive results in three tests, the increased diastase content of the urine, Loewi's adrenalin test, and the presence of glycosuria affords strong evidence that the pancreas is at fault ; (3) if there is also creatorrhoea and steatorrhoea, the suspicion of pancreatic insufficiency is confirmed ; (4) the tests have not supplied any evidence of gross disturbance of pancreatic function in diabetes mellitus ; (5) the following tests are of no value in the diagnosis of pancreatic disease and should therefore be discarded : the methods of estimation of trypsin and diastase in the oil-test meal and faeces, the Sahli test, Kashiwado's modification of Schmidt's test, Cammidge's pancreatic reaction, and Winternitz's sajodin test.

Cockcroft reports two cases showing the value of Loewi's adrenalin test as a sign of pancreatic insufficiency. In the first case, in which the pancreas was completely free from disease and quite efficient, the reaction was completely negative on three separate occasions, whereas in the second case the organ was almost completely destroyed.

Local discoloration of the abdominal wall as a sign of acute pancreatitis is described by Turner, of Newcastle-on-Tyne, who has observed it in two cases and attributes it to the direct action of the pancreatic juice which escapes via the retroperitoneal tissue and passes by the most direct route to the surface. In one of the cases in which the discoloration was noted round the umbilicus only the secretion may have reached that area via the round ligament of the liver.

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## SPINAL, REGIONAL, AND LOCAL ANAESTHESIA

The following account of communications on spinal, regional, and local anaesthesia is in continuation of the previous review (*Medical Science*, 1920, **2**, 161). The successful administration of general anaesthetics under the guidance of special anaesthetists, which prevails in this country, is in marked contrast to the depreciation of the procedure in other countries. The result of this depreciation is seen in the recourse to injection of toxic drugs in a variety of combinations and in various ways. The methods have much enlarged the field of experimental pharmacology, and patients submit because impressed by the statements as to the dangers of general anaesthesia.

A discussion took place at Vienna in June 1920, von Eiselsberg presiding, during which various opinions on local and general anaesthesia were advocated.

Finsterer stated that general anaesthesia had been disused in Vienna owing to the number of deaths under chloroform, 130 had occurred in Vienna in ten years. Hence, for example, in Dollinger's Klinik at Buda Pesth, it had come about that only 5 per cent. of the operations were being done under general anaesthesia. But most of the deaths were not really attributable to the general anaesthetic, and in the hands of special anaesthetists the danger had become very small. Moreover, deaths from pneumonia following operations occurred where no general anaesthetic was given. Nevertheless, Finsterer was an advocate of regional and local anaesthesia. 1,300 laparotomies had been done under local anaesthesia with the assistance of a little ether. Among 375 severe gastric operations there had been only 6 deaths within the first 24 hours; 3 were already exsanguine; 1, with cirrhosis of the liver, had recurrent haemorrhage; in 1 an apoplectic stroke was repeated. In only 1 stertorous breathing followed subcutaneous injections, first of morphine and atropine, next of novocaine, along with inhalation of a little ether. The patient died within 24 hours.

Denk, from experience gained in von Eiselsberg's Klinik, whilst not an opponent of local and regional anaesthesia, had collected together a great number of drawbacks. Cocaine he rejected altogether, tropacocaine should only be used for lumbar spinal anaesthesia, novocaine was by no means harmless owing to variation in the rate of absorption and its more active influence on anaemic patients. A weak solution of 0·5–1 per cent. may be administered so that the dose does not exceed 1·25 gm. of novocaine, but the dose of the 2 per cent. solution should be restricted to 40 c.cm., e. g. 0·8 gm. of novocaine, owing to the more rapid absorption. A number of cases were quoted bearing on this. Nephritis had been set up as well by novocaine, as by stovaine, and by Jonnesco's stovaine and strychnine combination. Albuminuria and casts are also found, the albumin up to 0·5 pro mille, which is transient if the kidneys are healthy beforehand, but pre-existing nephritis is made worse. After lumbar anaesthesia in a diabetic there was 4·5 pro mille of albumin. Alypin is more harmful still, and a small dose may be the direct cause of death. An injection of adrenalin has been the direct cause of death. After the injection of 10–12 drops of the 1 in 1,000 solution into an enlarged turbinal bone, there was sudden pallor, and permanent arrest of the heart and respiration. 15 drops of the solution injected as a preliminary to excision of the tonsils caused a similar sudden collapse and death. In a man under chloroform anaesthesia the injection of 10 drops into a turbinal had the same immediate fatal effect. Besides, adrenalin has set up local necrosis; extensive necrosis of the jaw, gangrene of toes, gangrene of the scrotal skin, of the skin of the penis, of the foreskin. Eucupine has proved especially harmful and has been discarded. The subsequent pain under a local anaesthetic is especially severe and prolonged after operation on the fingers.

Lumbar spinal anaesthesia has been attended by complications, whether stovaine, tropacocaine, or novocaine is used. Intense and prolonged headache, sleeplessness, also fainting, stiff neck, and vomiting, paralysis of the external rectus—all occur. Among 22,717 cases there were 92 of severe collapse and 12 in which the respiration was arrested. Among 9,322 cases of tropacocaine injection there were 7 deaths; among 14,741 of stovaine there were 25 deaths, and under novocaine 3 deaths. Several other lists have been published in which the deaths have varied between 1 in 200 and 1 in 500. Some of the cases have had suppurative meningitis, partial paraplegia, or local patches of gangrene.

Sacral anaesthesia is an uncertain procedure owing to the small size of the sacral canal, the uncertainty as to the dose required, and the possibility of immediate toxic effect by injecting into a vein. There is, besides, the danger of necrosis of the skin at the site of puncture.

The paravertebral method involves numerous punctures and a large amount of injection. It has proved chiefly dangerous in cervical injections for goitre and for thoracic operations.

The special dangers of the brachial plexus anaesthesia are the pain in the pleura, the complications following puncture of the pleura and lung, also the paralysis of the diaphragm following injection of the phrenic nerve. A limited persistent paralysis of the hand has followed.

Severe collapse has followed splanchnic injections; 1 in 6, 2 in 40, 2 in 300, have been reported. There are, besides, the dangers following intravenous injection, intentional or otherwise.

Although the conclusion is only a general one, because the condition of many of the patients was bad, yet it is impossible to assert that the foregoing procedures are without danger.

In the discussion which followed the reading of papers by Finsterer and by Denk, Sauerbruch said that he gave a general anaesthetic whenever possible, the psychical state of the patient being the main consideration. Schmid, from experience in the Gynaecological Klinik at Prague, held that lumbar spinal anaesthesia increased peristalsis of the intestines after the operation, which he considered due to the paralysis of inhibitory fibres in the rami communicantes. Kutscha, after employing splanchnic anaesthesia in 75 cases, was opposed to the method because of 4 cases of temporary collapse and 8 cases of gastric atony. In Wertheim's Klinik between 1910 and 1919 there had been 2,657 operations under general anaesthesia, and 2,583 under lumbar spinal anaesthesia, 70 per cent. of which were good throughout, 20 per cent. had to be helped out by a general anaesthetic. There was one death after using stovaine, and one after tropacocaine. There were 11 cases of severe temporary asphyxia and collapse, 2 of temporary unconsciousness and convulsions, 3 of meningitis, and 4 of temporary paralysis of the external rectus and legs. Headaches generally occurred, which were prolonged in 18. No case died directly of pneumonia, but 20 cases which died of pelvic inflammatory complications were found *post mortem* to have also lobular pneumonia. Albrecht rejected the systematic adoption of local anaesthesia. He carefully administered 90 per cent. ether with 10 per cent. chloroform, after a preliminary injection of morphine and atropine. Among 850 cases there had been no anaesthetic complication. Schnitzler said that the dangers of a general anaesthetic were altogether exaggerated, and he opposed Finsterer's favourable account of local anaesthesia. Lorenz had returned to general anaesthesia; many things could be done under a brief administration ; great harm was being done by physicians and general practitioners without special experience, who prejudiced patients against general anaesthesia. Jerusalem said that in Bier's Klinik the lumbar spinal anaesthesia followed the French method of mixing the drug with the aspirated fluid and re-injecting, tropacocaine being used. In Hochenegg's Klinik in 1911 90 per cent. had been operated upon under general anaesthesia, in 1920 only 40 per cent., especially for atypical operations and in the presence of inflammation. But the 60 per cent. under local anaesthesia were supplemented whenever necessary by brief administrations of ethyl chloride or of ether.

**Immediate death following suprarenin injection.** A nurse who had been ordered to inject 10 c.cm. of a 1 per cent. novocaine-suprarenin solution, injected instead 10 c.cm. of the 1 in 1,000 suprarenin solution into the skin and muscles of the thigh of a man aged 35. The man died within six minutes; there was nothing found to account otherwise for the death. Fisher, in recording the case, mentioned animal experiments by Ritzman. which showed that upon the subcutaneous injection of suprarenin, 6 per cent. entered the blood-stream, and 94 per cent. remained unabsorbed. On this basis the above case was killed at once by the entry into the circulation of 0·6 mgm. of suprarenin. Now to account for the deaths mentioned by Denk which occurred immediately after the injection of 10 drops and of 15 drops into a turbinal, it is only necessary to assume that the drug entered large venous dilatations; 20 drops = 1 c.cm. contains 1 mgm. of adrenalin; 10 and 15 drops contain 0·5 mgm. and 0·75 gm. respectively: 1 c.cm., or 20 drops, is usually held to be a maximal dose for subcutaneous injections, and that is $\frac{1}{10}$ of the dose which poisoned Fisher's case, but it must not be injected even into a small vein.

Meyer noted the toxic effects of a novocaine and bicarbonate solution when injected into a vein. The complications occurred when the injection followed directly on the puncture without paying attention to the return of blood through the needle. The toxic symptoms followed immediately upon the introduction of 5–7 c.cm. of the 1 per cent. novocaine bicarbonate solution, and consisted in sudden unconsciousness, pallor, arrest of breathing, dilatation of the pupils, also a general epileptiform seizure with foaming at the mouth. After 15 seconds or more the fit ceased, and this was followed by a deep inspiration. In the cases noted there was recovery sufficient for the operation to be proceeded with, analgesia being present, or some general anaesthesia being also required. The toxic effect had been confirmed by animal experiments. One case occurred in a young woman with a large goitre, in two the 2nd division of the 5th nerve was being injected, the point of the needle being in the pterygomaxillary fossa, preliminary to operations on the upper jaw. In a fourth case a paravertebral puncture penetrated a vein; the patient recovered after 20 minutes and the removal of a goitre was carried out. In the fifth and sixth cases, following on paravertebral injections preliminary to laparotomy, there was severe collapse, necessitating artificial respiration. Total analgesia followed, under which the operations were done. In both about 40 c.cm. of a 2 per cent. novocaine solution had been injected.

Hering described four cases apparently due to the injection entering a vein, as noted by Meyer:

(1) A paravertebral injection was being made preliminary to operating on a malignant goitre. After injecting one side, on commencing the injection on the second side the patient became suddenly unconscious, with deviation of the eyeballs, spasmodic twitchings of the face, and deep respirations. The pulse remained good; the spasms lasted three minutes, then consciousness returned, and the patient soon recovered. The interrupted operation was carried out some days later under the same anaesthesia without incident.

(2) A paravertebral injection was being made preliminary to operating on a goitre with slight symptoms of hyperthyroidism. The patient suddenly became pale, felt giddy, had oppression of the heart. This was considered 'psychical', and the injection on the opposite side being proceeded with, the patient became as pale as a corpse, the pulse very small and quick, the respirations superficial and irregular, and there was a severe outbreak of sweat The patient did not recover until the evening.

(3) Paravertebral injections were made before the resection of ribs for a pleural empyema. Immediately upon the injection there was severe collapse, the patient became as pale as a corpse, and failed to reply; the pulse was very small and quick, the respirations superficial, and there was severe sweating. This lasted half an hour, after which the patient had so far recovered that the operation could be proceeded with.

(4) Paravertebral injections were being made before operating on a bronchial fistula. At the sixth injection there was sudden collapse, the pulse quick, very small and fluttering; the respirations weakened and then stopped. The heart stopped within a few minutes. Artificial respiration and massage of the heart failed. No signs of puncture of the spinal cord were found; there were slight evidences of status lymphaticus the lymph-follicles at the base of the tongue, in the ileum, and in the spleen being considered a little swollen. The affected lung was adherent to the chest wall.

(5) Was a similar case to the foregoing so far, but as breathing continued some ether was administered and the operation proceeded with. But the patient did not recover from the collapse and died in 36 hours.

Schaps defined the danger from cocaine as dependent upon a certain amount of unaltered cocaine reaching the brain. This might happen when an average dose for subcutaneous injection entered a vein; also there was very rapid absorption of cocaine from certain mucous membranes such as that of the bladder, or from a serous membrane such as that of the tunica vaginalis. The reduction of the strength of cocaine solutions, e.g. to 1 in 1,000, necessitated the injection of a much larger amount of fluid, a longer time for the injection, much pain was caused, and the anaesthesia was very imperfect. Besides, the cocaine solution was not readily sterilized, the solution kept badly and septic complications followed. The best substitute, novocaine, had not more than $\frac{1}{3}$ of the anaesthetizing properties of cocaine, but at most $\frac{1}{10}$ of its toxicity. The attempt to increase the effect by using Esmarch's band involved other drawbacks; the employment of suprarenin, by lowering the blood-supply and vitality of the tissues, rendered a dilute solution of novocaine more efficient. Moreover, by delaying absorption, the suprarenin prevents local diffusion and checks any tendency to a toxic influence on the central nervous system. So long as there is no rapid absorption of novocaine by way of a vein the only complication likely is due to the injection of such nerves in the neck as the vagus or sympathetic. A quickening of the pulse, mostly due to emotional excitement, may be ascribed to the suprarenin. Reviewing published accounts of fatal cases, there are possible effects of preliminary scopolamine and morphine injections, especially in presence of even slight conditions of status lymphaticus. In minor surgery there are dangers because the patient has not been in bed beforehand, and is not kept lying down afterwards.

**Subcutaneous injections.** Griffiths noted the following disadvantages to the use of novocaine as a local anaesthetic. He employed a 0·5 per cent. solution to which 5–10 minims of adrenalin were added. The injections were preceded by a subcutaneous injection of scopolamine and omnopon so as to render the patient dazed or extremely sleepy. The subcutaneous injection of fluid rendered the tissues oedematous, of a mucoid appearance, and unnaturally blanched, owing to the adrenalin, whilst muscular structures were not relaxed. If adrenalin was used there was less primary haemorrhage, but more danger of reactionary haemorrhage. Under novocaine alone there was more primary haemorrhage than when a general anaesthetic was used. A serous discharge occurred from the incision for 7–9 days, so that it was better not to use Michel's clips, but only widely interrupted sutures, between which the serum could escape. In some there is intense pain as the effect of the novocaine passes off. Insomnia afterwards was a regular feature, and intense headaches in some, also in some severe lumbar pain for which the operating table was blamed. There was thirst during the operation and flatulence the next day. Retention of urine was far commoner than after a general anaesthetic. There were nearly as many chest complications. Many cases appeared slightly jaundiced, but the faeces were normal and bile-pigments were never found in the urine. During the radical operation for hernia, there was pain when the neck of the sac was reached. Varicose veins were so reduced in size that some were apt to be overlooked. The sphincter was not relaxed when operating on piles.

**Local anaesthesia by quinine salts.** Brown disagreed with the general condemnation passed upon the use of quinine salts. For twelve years he had used local injections for tonsil and adenoid operations. The dose he employed was 1½ gr. of quinine hydrochloride in 2 drm. of water; he had at one time injected double the dose, since reducing it there had been no instance of oedema and sloughing. Half an hour beforehand 4–8 drops of a 0·1 per cent. solution of scopolamine was put under the tongue. Then, using swabs soaked in 20 per cent. cocaine, kept sterile by 1 per cent. phenol, the tonsils and pillars were well rubbed three times at intervals of 2–3 minutes. Finally, the above dose was boiled in a spoon and the syringe filled with the addition of 2–3 minims of epinephrin. The injections were made into the supra- and infra-tonsillar regions as well as into the pillars of the fauces, and after 10–15 minutes a perfectly satisfactory local anaesthesia was established and there was a complete absence of toxic complications. The effect was evidently a combined one and not the result of the quinine salts alone.

**Spinal anaesthesia.** Bumke, having had his attention drawn to the increase of complications following lumbar and spinal anaesthesia, reported recent experiences in the Klinik for Nervous Diseases at Breslau, following lumbar puncture for diagnostic purposes. Formerly, patients after lying down for half an hour could be sent home. Since 1918 it had become necessary to admit such patients to the hospital for two or three days on account of the frequency with which headache, malaise, and vomiting followed, complications which in some cases delayed to appear until the second or third day. Cases of multiple sclerosis, tabes, and latent syphilis were especially predisposed; but the above complications supervened in cases in which no organic disease could be found. Bumke was unable to explain the marked increase in frequency.

Baruch concluded that the toxic complications which follow injections into the spinal theca are due to the leakage out of the cerebrospinal fluid beside the needle into the subcutaneous and perithecal tissues. This he would prevent by using a very fine needle and puncturing whilst the patient is lying horizontal, whether on the side or face.

Richter analysed the 601 cases of lumbar anaesthesia observed since 1905 in the surgical department of a hospital in Karlstad, Sweden. The solution used was stovaine 0·08 gm., suprarenin boric. 0·00026 gm., chloret natr. 0·0022 gm., and aqua destill. ad 2 c.cm. Half an hour before the operation 1 cgm. of morphine was given. The technique of the injection followed conventional lines with this exception, that immediately after the injection the patient was placed in a horizontal position with his head propped up by a couple of pillows. Trendelenburg's position, as advocated by most writers, was never adopted. When anaesthesia was found not to be complete within fifteen minutes of the injection it was regarded as having failed. As a rule, the anaesthesia lasted for at least an hour, and partial anaesthesia persisted for a maximum of four to five hours.

Richter classifies his material according to the nature of the operation and the completeness of the anaesthesia. Under the heading Incomplete Anaesthesia he includes all the cases in which the patient complained of pain, or in which it was found desirable to administer ether before the completion of the operation. Included under this heading were some nervous patients who complained of, although they probably did not suffer from, pain. In some cases the anaesthesia was complete in the greater part of the field of operation, but when, for example, a rectal amputation was followed by a colostomy, this last stage sometimes proved to be painful. In other cases the anaesthesia began to pass off before the operation was completed. A certain proportion of failures was traceable to the inexperience of the operator or the staleness of the anaesthetic. The anaesthesia was incomplete in 5·8 per cent. of all the operations. These partial failures occurred chiefly in connexion with colostomies, prostatectomies, hysterectomies, castrations, &c. In 33 per cent. of the vaginal hysterectomies, 18·5 per cent. of the castrations, 24 per cent. of the transvesical prostatectomies, and 33 per cent. of the amputations of the rectum with colostomy the anaesthesia was incomplete. On the other hand, this was the case only with 2 out of 66 amputations of the thigh, and all the 22 amputations below the knee were conducted under complete anaesthesia. Serious consequences of lumbar anaesthesia such as cessation of the pulse and respiration, paralyses and trophic disturbances were never seen, and no death was traceable to the anaesthetic. Only in a few cases did the patients experience slight malaise or vomiting. Probably this freedom from serious ill effects was due to the quality of the anaesthetic, the avoidance of Trendelenburg's position, and the principle adopted of not attempting operations under lumbar anaesthesia on the upper segments of the body.

These original observations are supplemented by a summary of the experiences of 34 writers. Their combined material consists of 26,446 cases observed in the period 1917–20. Among these there were 12 deaths, i. e. a mortality of 0·045 per cent. Richter shows that all these writers are more or less enthusiastic in their advocacy of this form of anaesthesia, but he notes that some, like himself, recommend it only for operations below the umbilicus. Stovaine and tropacocaine appear to be equally popular, whereas novocaine is less used. Scrutiny of the fatalities showed that practically all the patients were from the outset in a critical condition; they suffered from peritonitis, intestinal obstruction, chronic morphine poisoning, or other debilitating influences. Most writers seem to stress the harmlessness of this method provided adequate precautions are taken. Richter endorses this generalization, but he does not advocate lumbar anaesthesia for every operation on the lower part of the body because with recent advances in the technique of local anaesthesia this is often to be preferred. But when rapid anaesthesia is required, for example, after accidents, and a delay of 15 to 20 minutes is of consequence, lumbar anaesthesia, with its almost instant effect, may be indicated. It is also indicated when the action of local anaesthesia is likely to be uncertain, and the patient is for some reason or other disqualified for general anaesthesia.

**General analgesia by cocaine injected into the spinal theca.** This is a method especially practised in France by Le Filliatre and Delmas. Delmas employed cocaine hydrochloride, the preparations being sterilized in the cold and preserved solid in tubes. The dose is mixed with cerebrospinal fluid sucked out from a low lumbar puncture, and after being dissolved in the fluid is forcibly reinjected. A general analgesia is produced immediately; in 600 cases there were no complications, the only precaution being that the patient should not be raised for 24 hours. In a clinical lecture a year later Delmas treated the above method as if it were one for general adoption. Le Filliatre followed the same method, but half an hour before the spinal injection, he gave a subcutaneous injection of scopolamine, morphine, strychnine, and sparteine. The dose of cocaine hydrochloride employed was for the lower limbs 1·5 cgm., for analgesia up to the umbilicus 2 cgm., and above 2·5 cgm., or for a strong man 3 cgm. Cerebrospinal fluid was first let off, for analgesia up to the breast 20 c.cm., if it escaped in drops, if in jets 25 c.cm., for analgesia to include the head 5 c.cm. more. 2–3 c.cm. was reinjected after dissolving the dose of cocaine. An assistant is required to make the patient breathe regularly at 20 to the minute, and to sponge the face repeatedly with cold water. The patient could be placed in the Trendelenburg or any other position, but the head must not be raised during the operation or after it for two hours. Drink was given two hours after the operation and food ten hours after. 3,000 such injections for analgesia had been made without accident; of 195 consecutive operations between October 1918 and January 1919, in only one had a general anaesthetic, viz. ethyl chloride, been adopted, and that on account of lumbo-sacral cellulitis. These included 7 operations on the head, 4 on the neck, 19 on the upper limbs, 15 on the thorax, 61 on the abdomen, 7 in the dorso-lumbar, and 7 in the ano-sacral region, with 58 on the lower extremities. The average duration of the analgesia for the head and neck was ¾–1 hour, and the return of sensation was slow, on an average 8 hours. There was no occasion for morphine after the operation. There were no failures, headaches, or vomiting, either during or after the operation, no consecutive paralyses or retention of urine. In 2 per cent. slight irregularity of the respiration and a weakening of the pulse followed the injection, but this lasted not more than 5–10 minutes.

Riche used the French form of novocaine called synkain, an 8 per cent. solution without admixture of adrenalin. The dose used was 1 cgm. synkain per 5 kilos body-weight; e. g. 14 cgm. synkain for a body-weight of 70 kilos. After removing 10–25 c.cm. of cerebrospinal fluid, the dose was mixed with the escaping fluid and immediately reinjected at the rate of 0·1 c.cm. per minute. Since 1914 the injection had been used for 1,000 operations without any fatality or severe complications, during which period a general anaesthetic had been given 50 times. In 4 cases there had been hemianalgesia, in 3 a temporary respiratory disturbance. About 30 had exhibited pallor and a slowing of the pulse below 60, with vomiting. The following day many had headache and two biliary vomiting.

**Paravertebral injections.** Rick, of Marburg, used paravertebral injections in 100 gynaecological cases. It was essential to induce twilight sleep by veronal, scopolamine, and narcophine in 3 preliminary doses, the influence of which continued for some 5¾ hours. Then about 70 separate injections of 5 c.cm. each were made, using a 0·5 per cent. novocaine-suprarenin solution, the total being limited to 450 c.cm. The injections occupy 35–40 minutes and involve 20 separate punctures. The nerves injected were the 6–12 dorsal and the 1–3 lumbar for abdominal operations; for operations below the umbilicus from the 8th dorsal; for pelvic operations from the 11th dorsal.

The difficulty experienced was the contraction of the back muscles as the point of the needle was directed forwards to the side of the vertebra. The kidneys may be punctured as shown by haematuria; in one case a presacral postrectal abscess was set up.

Preiss, in a communication dealing with the paravertebral injections described by Kappis, commenced with a description following Langley of the autonomous, sympathetic, vegetative or visceral nervous system, and reached the conclusion that all real sympathetic nerves are efferent or motor. The afferent nerves, with which alone the question of blocking to create anaesthesia is concerned, have their trophic centre in the spinal ganglia. Grey rami communicantes passing out from spinal ganglia split up and terminate around ganglion cells, whether of the vertebral chain or of the prevertebral ganglia. The paravertebral injections are directed to block the afferent visceral fibres between the prevertebral and the spinal ganglia. The upper abdominal visceral afferent nerves travel to the spinal cord by way of the nervi splanchnici major and minor, which pass through the diaphragm between the lateral and central crura, having the vena azygos on the right and the vena hemiazygos on the left.

The afferent nerves from the lower abdominal viscera may be blocked by injecting at the level of the 3rd lumbar intervertebral disk. As regards the segmental arrangement of these abdominal visceral sensory fibres, no method of injection can be based upon it alone, for there is much additional spreading and crossing.

Experiments on the cadaver of injecting by the procedure described by Kappis and using methylene blue, demonstrates that through two punctures on each side it is possible to block all the abdominal afferent nerves. One puncture at the level of the 12th interarticular cartilage serves for the infiltration of the paravertebral loose connective tissue around both splanchnic nerves, above and below the diaphragm. The second puncture at the level of the 3rd lumbar intervertebral disk serves for the infiltration of the paravertebral connective tissue from the level of the 2nd lumbar vertebra to the promontory, and blocks the lower abdominal afferent nerves.

In making the upper injection the needle is entered 7 cm. from the tip of the spinous process so as to pass forwards immediately underneath the 12th rib; it is directed inwards and forwards towards the middle line at an angle of 30° to the vertical plane until the point touches the side of the 12th intervertebral disk. Next, the needle is pushed forwards farther to the level of the front of the vertebra. It is then necessary to establish that the point is not in a blood-vessel by finding that blood is not drawn out through the needle. This done the injection is made. The procedure is repeated on the opposite side, also at the two points corresponding to the 3rd lumbar intervertebral disk. Thus four punctures in all are made. A more thorough infiltration may be made at each puncture by injecting only one-third of the dose in the horizontal direction, then directing the point of the needle upwards for 2 cm. at an angle of 30° to the horizontal, and afterwards downwards for 2 cm. at the same angle. The injection upwards and downwards of one-third extends the area of diffusion. But whenever the point of the needle is moved, it must be first proved that blood cannot be aspirated, before the actual injection is made. Moreover, care must be taken not to move the point when fixing on the syringe and whilst making the injection.

The foregoing method blocks the afferent visceral fibres, but not the afferent fibres of the abdominal wall. Hence it is necessary to infiltrate the abdominal wall widely down to the parietal peritoneum, and this must be done thoroughly or the patient will complain bitterly when retractors are applied or when gauze packs are inserted after opening the abdomen. Among 150 abdominal operations under the above injections 23 required the assistance of a general anaesthetic.

**Splanchnic anaesthesia.** Reichle reported on 8 cases in which splanchnic anaesthesia had been adopted. In 5 there was a partial excision of the stomach, in 1 jejunostomy, in 1 gastro-enterostomy, and in 1 appendicectomy. The anaesthesia was good in 5, in 1 poor, and it failed in 2. Four of the cases had post-operative pneumonia.

Paul, for gastric operations, had formerly given a preliminary injection of morphine, and then injected the abdominal wall. The morphine had been dispensed with in order to preserve reflex excitability. Scopolamine had been tried, but the deep somnolence produced was attended by cyanosis and shallow respiration. The injection of the abdominal wall proved unsatisfactory and ether was given until the abdomen was opened. Then a 0·5 per cent. novocaine solution with suprarenin was injected into the gastro-hepatic omentum and root of the mesentery, after which the operations were carried out. But the patients were liable to sudden pallor, rapid pulse-rate, and retching, whilst the anaesthetic effect was very short.

Schmilinsky, in 45 gastric operations under splanchnic anaesthesia, preceded by scopolamine and morphine subcutaneously in order to avoid a general anaesthetic, experienced difficulties owing to the mental excitement of the patient, and from retching. In the discussion Kümmell urged caution with the method in face of possible dangers.

**Sacral anaesthesia.** Zweifel discussed 10 cases which had died after injections into the sacral canal, among which three deaths appeared due directly to the injection, death in the other cases being attributable to other causes.

i. A woman underwent total hysterectomy for a myoma, and five days later an artificial anus was made under sacral anaesthesia for the relief of intestinal obstruction. Cyanosis set in one hour after the operation and she died two hours later.

ii. A woman had the neck of the uterus removed under twilight sleep followed by sacral anaesthesia. She collapsed and died eight hours after the operation.

iii. A patient had twilight sleep and sacral anaesthesia preparatory to laparotomy for tuberculous peritonitis. A few seconds after the sacral injection the respiration stopped and death followed.

iv. A woman in her fourth labour had twilight sleep followed by sacral anaesthesia. Then extraperitoneal Caesarean section was proceeded with, but the patient died before the end of the operation.

v. A patient with a perforated gastric ulcer and general peritonitis had a sacral injection ; death occurred 20 minutes later, without the laparotomy having been commenced.

vi. Sacral anaesthesia was adminstered before the extirpation of a carcinomatous uterus. Stupor and ocular paralysis supervened, followed by death six days after the operation.

vii. A patient extremely anaemic owing to a uterine myoma had a sacral injection ; the respiration and heart stopped and death occurred 10 minutes after the injection.

viii. A woman with an exophthalmic goitre had a sacral injection before extirpation of the uterus. Five minutes after the commencement of the operation, ether had to be administered and death occurred before the operation was completed, one hour after the injection.

ix. For prolapse of the uterus a subcutaneous injection for twilight sleep was followed by a sacral injection ; seven minutes after the latter the patient died.

x. A case died after sacral anaesthesia for a pelvic operation, but internal haemorrhage had also occurred.

Schmerz, among 65 operations, had 55 ideal results from high sacral anaesthesia. One man of 65 died suddenly just as the coccyx was being removed preliminary to an excision of a rectal cancer ; a woman, during an operation for strangulated hernia, had convulsions and died. In 3 the injection failed, in 2 it was incomplete ; the remaining 5 had temporary complications, spasms, want of breath, shock, loss of consciousness, and in 3 of them epileptiform spasms with biting of the tongue.

**Kulenkampf's anaesthesia of the brachial plexus.** Capelle added to the list of dangers involved in the practice that of paralysing half the diaphragm, owing to the injection of the phrenic nerve. Also he recorded a fatal case. In a man aged 72 with suppurative tenosynovitis of the left hand, the brachial plexus was injected with a 2 per cent. novocaine and adrenalin solution. This set up complete collapse of the left lung with pneumothorax and surgical emphysema. Broncho-pneumonia supervened and death followed in two days.

In Hering's case a fatal pneumothorax was set up. A man aged 52 had become exhausted by sepsis from the left 4th finger, which, in the course of a fortnight, had extended along the tendon sheaths into the forearm. Under plexus anaesthesia incisions were made in the palm and forearm : five days later, under the same anaesthesia, the forearm was amputated. Signs of pneumothorax were noted after the first operation, and dyspnoea increased until death. The lung on the side of the injection was completely collapsed—it presented several small abscesses; the puncture made by the injecting needle in the dome of the pleura was found. There was, besides, an abscess in the fat over the left lobe of the thyroid, and bronchopneumonia in the opposite lung.

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## GRAFTS OF DEAD TENDON

It is obviously convenient to use for grafts dead tendon material which has been preserved in requisite lengths free from sepsis. French surgeons have successfully repaired extensive losses of flexor and extensor tendons of the hand with it. Nageotte proposed as material, tendons of embryo calves which could be got when cows were being slaughtered. Each tendon can be taken out, using aseptic precautions, and kept on a stretch by tying it to a glass rod with aseptic ligatures. The tendon on the rod is put into 90 per cent. alcohol, changed after ten days into 60 per cent. alcohol, in which it is permanently preserved. The alcohol being first soaked out in warm sterile serum or salt solution, the tendon has been successfully used after being kept for 17 months. Tendons from dogs have been also employed after preservation in the same way.

Nageotte and Sencert operated on a soldier who, in March 1918, was wounded by a fragment of shell on the palmar surface of the wrist. Acute suppuration followed and several incisions had to be made. In June there was still free suppuration, with an elevation of temperature, swollen axillary glands, and the hand flexed at the wrist like a claw. Over the palmar surface of the wrist was a diffuse swelling with sinuses. These were laid open, flexor tendons exposed, granulations scraped away from the tendon sheaths and the wound plugged with gauze. In the course of the next six weeks flexor tendons sloughed away and the wound healed. This left the four fingers flexed completely into the hollow of the palm. It was impossible to straighten out these fingers. In August a median incision was made on the palmar aspect 10 cm. in length; by further longitudinal incisions the scar tissue which had replaced the lost tendons was cut out, and the ends of the persisting tendons defined. After the fingers had been fully extended, there was a gap between the ends of the tendons of the flexor sublimis and flexor profundus digitorum, except that the tendon of the flexor profundus to the little finger could be dissected out intact from the scar and partly also the corresponding tendon of the sublimis; in the six other tendons there were gaps of 3–4 cm. each, which were filled by six tendons of 3–3·5 cm. in length. These had been taken from dogs and preserved for a month in alcohol. The dead tendons were each fixed to the pared corresponding ends of the living tendons by two catgut sutures. Over them were separately sutured the deep fascia and then the skin without drainage. Healing occurred by first intention and three months later there was complete extension of all the affected fingers. The flexion of all the phalanges of the affected fingers was almost complete, except the middle finger, in which there was some limitation of flexion.

Delorme examined the man and found that when the proximal phalanges of the index, middle, and ring fingers were held fixed in extension at the metacarpophalangeal joints, the flexion of the middle upon the proximal phalanx was active and almost complete, which indicated that the tendons of the flexor sublimis had been restored to continuity. When the middle phalanges were held extended, the ungual phalanges could be actively flexed on the middle, almost to the normal degree, showing that the tendons of the flexor profundus had been likewise restored.

Durand reported three cases in which the foetal calf tendon had been used:

(1) An infantryman at Verdun was wounded by a shell on the inner side of the right forearm, three fingers' breadth below the epitrochlea, in January 1918. Being taken prisoner, he was first treated in Germany. In June 1919 he was found to have complete flexion of all three phalanges of the index finger, and there was a foreign body lodged in the line of the radial artery two fingers' breadth above the wrist. The foreign body was removed, but the contraction of the index finger persisted. In August it was found on exploration that the one tendon injured and the cause of the contraction was the tendon of the flexor profundus to the index finger. When the scar was excised and the finger extended there was a gap of 6 cm., which was filled in by a similar length of foetal calf tendon. The finger was kept fully extended until after healing by first intention; passive and active movements were begun in the third week. In the following October the index finger could be completely extended and there was no sign of the recurrence of any tendency to contract. As to flexion this was complete, so far as the flexor sublimis action on the middle phalanx was concerned; as to the active flexion of the ungual phalanx by the restored tendon of the flexor profundus, this was definite but limited.

(2) A man of 59 had, twelve years before, ruptured his left biceps. In April 1920 he strained the same arm and felt a pricking sensation on the outer third of the dorsal aspect of the left hand. In May, after another strain, he was unable to extend the terminal phalanx of the thumb. It was found that the long extensor, extensor secundi internodii pollicis, failed to act; the other two extensors acted well. An incision was made in the line of the ruptured tendon and the ends found separated, so that after they were refreshed the gap between them measured 4 cm. This was filled by a foetal calf tendon which had been preserved in alcohol for a year. The sheath, which had not been destroyed, was sutured over the graft. Healing occurred by first intention; passive movements were begun after 10 days. The man, when exhibited, could fully extend the ungual phalanx of his thumb.

(3) A soldier, in July 1918, whilst a prisoner in Germany, received a deep cut in the metacarpophalangeal fold of the fourth and fifth fingers of the left hand. The wound healed with absolute fixation of the tendons in flexion. In July 1919 the superficial and deep tendons were dissected out; they had become densely adherent for 1·5 cm., the sheaths for that extent being destroyed. Only one graft was used for uniting both superficial and deep tendons. Healing by first intention occurred, but there was no functional improvement after two months. This was attributable to one graft only being used for the two tendons and to the destruction of the synovial sheath over the metacarpophalangeal joints, so that adhesions recurred fixing the grafted tendon.

Chaton reported two observations:

(1) In a man, aged 20, a gunshot injury had completely divided the extensor tendons of the four fingers; the fingers had become flexed into the palm, and stiff, especially at the metacarpophalangeal articulations. In January 1919 dead tendon grafts, 4–5 cm. in length, were inserted. By the following June the patient could with ease flex to a right angle the second and third phalanges upon the first phalanx, and then make a complete active and forcible extension to the full. The flexion could not be carried further because the metacarpophalangeal joints were definitely ankylosed.

(2) A soldier, following a septic puncture, had destruction of the flexor tendons of the right middle finger. As the finger had become fixed in complete extension, the man asked for it to be amputated. In April 1919 the long palmar cicatrix was excised down to the bone; the proximal ends of the tendons were defined at the end of the palm. First a dead tendon 8 cm. in length was sutured to the proximal end of the profundus tendon and to a tongue remaining at the insertion of the tendon into the ungual phalanx. The sublimis tendon was reconstituted by a similar length fixed to the refreshed proximal end and at the middle of the second phalanx to remnants of scar tissue attached to the bone on either side. Slight inflammation followed for ten days; passive movement was begun on the eighth day. At the end of six weeks the finger could be voluntarily flexed to 45° at the proximal interphalangeal joint, but the distal interphalangeal joint could not be flexed by the flexor profundus. Therefore ten weeks after the above insertion of dead grafts, these were exposed and found fully preserved, but adhering together at two points. The adhesions were separated and the grafts kept apart by inserting sterilized animal membrane. Passive movement was begun on the second day after this second operation; some suppuration followed: active movement was not regained; the patient again demanded amputation, which was done. On dissecting the finger, the grafts were found as fixed by the sutures, not absorbed. They had a pearly appearance, as of normal tendon. Adhesions had recurred at the sites of suppuration.

Sauvé used dead tendon grafts for a boy aged ten, whose right wrist had been bitten, so that he had lost the power of extending his index, middle, and ring fingers. In September 1920 the injured extensor tendons were widely freed and a graft 10 cm. in length inserted into each. The extensor indicis was furnished with a double graft, the end of the grafts being attached to the distal ends of the extensors of the index and middle fingers. This grafting was a complete success, all the fingers regained normal movement.

In the course of the discussion it was stated that Sencert had had only

2 failures out of 35. Jalifier, of Lyons, reported 5 cases of grafting dead tendons into the hand with good results.

Auvray, in his report on the communications by Chaton and Sauvé, said that he had inserted seven grafts to restore movement in the thumb and first four fingers, also seven grafts into the thumb and first two fingers as well as into the palmaris longus and brevis. Whenever possible, especially about the wrist, the sheaths should be preserved and sutured over the grafts; this is impossible more often in the case of the flexor tendons, and therefore there are better chances of restoring the extensor tendons.

Ombrédanne considered that success depended on the question whether the sheath could reproduce the tendon, the graft serving merely as an aid to the sheath in modelling a new tendon.

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W. G. S.

## THE ELECTROMYOGRAM IN NERVOUS DISEASES

The investigation of the action currents produced by skeletal muscles is likely to become an important method of research in organic neurology, and for this reason it seems worth while to summarize the information which is already available. The central fact is that during voluntary contraction the skeletal muscles give rise to an irregular, oscillating action current with a period of about 50 vibrations a second. These currents are very easily recorded by binding a couple of pad electrodes to the surface of the limb and leading from them to a string galvanometer with a photographic recording apparatus. The sensitiveness of the galvanometer need be no greater than that required for electrocardiographic work, and the standard electrocardiogram outfit can be used without alteration.

The nature of the ‘ electromyogram ’, as the oscillating current is called, was investigated in detail by Piper; he showed that the oscillations were easily explained in accordance with the generally accepted theory that the voluntary contraction is a tetanus maintained by a rapid succession of impulses from the motor nerve. This agrees with the fact that a muscle in voluntary contraction is not in a steady condition, but shows a rapid mechanical oscillation, and whereas it was formerly supposed that the rhythm of these oscillations did not exceed 20 a second, the recent observations of A. V. Hill indicate a rhythm of 40 to 50 a second, i. e. a rhythm identical with that of the electromyogram. We may take it, then, that in a normal subject the voluntary contractions are due to the passage of a rapid succession of impulses into the muscle, and that the frequency of these impulses can be determined by recording the electromyogram. But although in this way we can analyse the voluntary contraction into a series of simple twitches in the muscle, yet it does not follow that we can analyse the discharge from the central nervous system in the same way. The frequency with which impulses pass down the motor nerve from the spinal cord may be very much greater than 50 a second, and the muscular rhythm may be simply the maximum rate at which the muscle can respond to the more rapid sequence of impulses reaching it from the nerve. The experiments of Forbes and Rappleye make it almost certain that this must be the true state of affairs, though Piper and others have supposed the rhythm of the electromyogram to be identical with that of the impulses in the motor nerve.

At any rate, the rhythm is very rarely changed; the oscillations are too irregular to allow of exact measurement, but as far as can be seen an increase in the force of contraction increases the amplitude of the oscillations but does not affect their frequency, and the only conditions which do produce an alteration are (1) a change of temperature in the muscle and (2) extreme fatigue.

Whether any significant changes in rhythm appear in different nervous diseases is still an open question. Hitherto, no case of departure from the usual voluntary contraction rhythm of 50 a second has been described in any group of nervous diseases, but very little systematic work has been published. On the other hand, a considerable amount has been done on the nature of the action currents in the reflexes and in conditions of increased tone.

In regard to the tendon reflexes the position seems fairly straightforward. Wertheim-Salomonson, Hoffmann (1), and others have shown that in the knee-jerk the reflex contraction of the quadriceps is accompanied by a single diphasic action current which has the same form as that produced by stimulating the motor nerve with a single shock. The latent period is naturally longer for the reflex effect, but the immediate cause of the contraction must be the same in both cases, namely, the passage of a single impulse down each motor nerve-fibre. The same type of response is found in all the tendon reflexes, a single diphasic action current after a latent period slightly longer than that obtained by stimulating the motor nerve. Clearly we have to deal with a very simple type of reflex mechanism, but what the biological significance of the reflex may be is not so clear. Why should every muscle respond with a single reflex twitch when its tendon is tapped? The usual explanation is that the tendon-jerk is a protective reflex which prevents a sudden overstretching of the muscle, but some recent work of Hoffmann (2) and Preisendorf suggests that it may play a much more important part in the general regulation of movement. Their work deals mainly with the relation between the tendon reflexes and voluntary contraction. They find that if a rapid series of weak tendon reflexes is produced by electrical stimulation of the motor nerve or by intermittent traction on the muscle, the simultaneous occurrence of a voluntary contraction leads to a great increase in the electric response which accompanies each tendon reflex; if the frequency of the tendon reflexes is great enough the electromyogram of the voluntary contraction appears as a regular series of diphasic responses synchronizing with the tendon reflexes, and the usual irregular 50 a second rhythm is completely absent. In these conditions the voluntary contraction appears to be nothing more than a series of augmented tendon reflexes. These have set the rhythm of the spinal arcs, and the effect of the discharge from the cerebrum has been to lower the synaptic resistance of these arcs and so to produce a more extensive response. Hoffmann regards the tendon reflex as the elementary reaction out of which the whole postural tonus of the muscle is built up, and he has brought forward a certain amount of evidence in favour of this view, although it is one which is not very easy to reconcile with other experimental and clinical evidence on the relation of tone and the tendon reflexes (Walshe).

Observations on the electric response in conditions of increased tone are, to some extent, contradictory, as indeed is most of our information about the tonic contraction, but the problem is so important that any fresh information must be welcomed by physiologists and neurologists alike. The position is complicated by the lack of any general agreement as to the definition of a tonic contraction; Sherrington has given a clear account of the conditions which must be fulfilled before a contraction can be spoken of as tonic, but these conditions are not always adhered to by other workers.

The position can best be understood in the light of prevailing theories as to the nature of tone. The most definite theory regards the tonic contraction as an entirely different affair from the tetanic, voluntary contraction—different in its innervation, its metabolism, and its muscular mechanism. According to this view the voluntary contractions and the phasic reflexes are due to impulses passing down the medullated nerve-fibres from the anterior horn cells of the cord; the mechanical effect is caused by the repeated excitation of the fibrillar mechanism of the muscle, it involves a considerable expenditure of energy derived from the breakdown of carbohydrate, and it is accompanied by a series of diphasic electric responses. The tonic contraction, on the other hand, is supposed to be due to the sarcoplasm of the muscle innervated by non-medullated fibres of the sympathetic system; it is not accompanied by any electric change, and it has a metabolism of its own involving very little expenditure of energy and possibly leading to the production of creatin as an end-product instead of $CO_2$ and $H_2O$ (Langelaan).

This theory has already formed the basis of far-reaching medical and even psychological speculations, but it cannot be said that the evidence for it is altogether satisfactory. There is no doubt that fibres from the sympathetic system appear to end in close connexion with skeletal muscle-fibres, and there are a number of observations on the form of the muscular contraction before and after destruction of the sympathetic ganglia which have been interpreted as implying a sympathetic innervation for the tonic element in contraction. But the two conditions which are usually regarded as typical examples of the tonic state in mammalian muscles are not so easily fitted into this scheme. These are (1) the long-continued contraction of a muscle which has been treated with veratrin, and (2) the state of decerebrate rigidity. In the former, after large doses, the contraction is maintained without any electric change, but the expenditure of energy is very large; the heat-production is said to be many times that developed in an ordinary tetanic contraction (von Frey). It is, however, one of the chief features of the tonic contraction that it is maintained with a very small expenditure of energy, and for this reason, if for no other, we can put little reliance on the analogy between the veratrin contraction and the physiological state of tone. Decerebrate rigidity has much more claim to be regarded as a typical example of the tonic state. Both heat-production and metabolism are very small, fatigue is absent, and the mechanical condition of the extensor muscles corresponds absolutely with that of the hypertonic muscles in a case of spastic paralysis (Walshe (2)). But in decerebrate rigidity the muscles show an oscillating electric response, and their contraction does not depend on a sympathetic nerve-supply. This suggests that decerebrate rigidity is a tetanus and as such is not essentially different from a voluntary contraction, although the activity must be confined to certain fibres which can work much much economically than the average. If this position be accepted it follows either that decerebrate rigidity is not a tonic contraction, or that tone is not due to a steady contraction of the sarcoplasm innervated by the sympathetic.

Wertheim-Salomonson accepts the former alternative; for him decerebrate rigidity is a tetanus and there are other forms of contraction more properly called tonic in which an entirely different mechanism comes into play. This distinction is based on the presence of the oscillating electric response in decerebrate rigidity and its absence in the other forms of contraction, and it must be admitted that the evidence from organic nervous disease favours this point of view, for hitherto most cases of spastic paralysis have failed to give any clear evidence of an oscillating electric response. Thus Hober found no action current in the paralysed arm muscles of a case of hemiplegia of two years' duration. In an old case of spastic paresis an oscillating action current was present when the arm carried out a feeble associated movement, but not when it was at rest. Wertheim-Salomonson finds no action current in the spastic muscles in hemiplegia, transverse myelitis, multiple sclerosis, &c., and Sanger and Bornstein find none in amyotrophic lateral sclerosis.

The very close resemblance between decerebrate rigidity and spastic paralysis in every other respect but that of the electric response makes it difficult to accept the idea that the two conditions are radically different, and those who feel this difficulty may console themselves with the argument that the oscillations found in decerebrate rigidity are small and might be missed altogether if the electrodes were applied to the intact limb instead of the isolated muscle. But this argument does not apply so well to other cases in which a tonic contraction is found without an oscillating action current. In the reflex contractions due to tetanus toxin, for instance, the oscillating current is absent in the late stages of the poisoning, although very sensitive recording arrangements have been used to detect it (Frohlich and Meyer). It is to be noted, however, that Liljestrand and Magnus find that destruction of the sympathetic ganglia has no influence on the reflex spasm due to tetanus toxin, so that in this case, as in that of decerebrate rigidity, the idea of a sympathetic innervation must be abandoned.

There is no doubt that these tonic contractions must be produced by a mechanism which differs considerably from that at work in the phasic reflexes, although the difference may be quantitative rather than qualitative, and the state of decerebrate rigidity may represent a half-way house between the two extremes. Clearly a great deal more evidence will be necessary before any definite conclusion can be reached, but the subject has attracted so much attention that it is unlikely that it will remain for long in its present unsettled state. For this and for similar problems the investigation of the electromyogram in nervous diseases is likely to be of the utmost importance.

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E. D. A.

## THE EXPERIMENTAL PRODUCTION OF ALTERATIONS IN BRAIN VOLUME

The researches of Weed and others on the anatomy and physiology of the cerebrospinal fluid circulation have already been reviewed in *Medical Science*, (1920–1, **3**, 160). An interesting and important addition has now been made by Weed and McKibben to these observations by their discovery that the intravenous injection of hypertonic salt solutions lowers the cerebrospinal fluid pressure and causes a marked diminution in the volume of the brain. Hypotonic solutions, on the other hand, cause swelling of the brain and a rise in cerebrospinal fluid pressure.

They employed cats for their experiments. The cerebrospinal fluid pressure was determined by means of a water manometer connected with the subarachnoid space by puncture of the occipito-atlantoid ligament.

They found that the average pressure recorded by this means was 120 mm. of water. Intravenous injections of from 20 to 50 c.cm. of 30 per cent. solutions of sodium salts (chloride, sulphate, bicarbonate), cause a rapid and persistent fall of this pressure to well below zero in some instances. In addition, the brain volume, observed through a trephine hole in the skull, visibly diminishes. Injection of sterile water, on the other hand, causes a rise of pressure to nearly 300 mm. of water and visible swelling of the brain. This swelling persists after decapitation. The fall of pressure after hypertonic injections persists for several hours, but the rise after hypotonic injections is more transient. They conclude that fluid is taken up by the brain in these circumstances by osmotic pressure into the perivascular spaces.

Foley and Putnam, at Cushing's suggestion, repeated these observations with a view to determining whether or not similar results could be obtained by the oral administration of the solutions, because it seemed probable that the withdrawal of fluid from the blood by this means might suffice. The observation might then be utilized for cranial operations, making them easier by lowering tension and diminishing brain volume. With intravenous injections they fully confirmed Weed and McKibben's findings, obtaining an even greater fall in cerebrospinal fluid pressure with hypertonic solutions. They then tried the effects of doses by mouth, by rectum, and by direct introduction of the solutions into a loop of duodenum. In every instance the effects were the same as those of intravenous injection. For example, a dog was given a massive dose of 180 c.cm. of a 30 per cent. solution of salt into the stomach. The cerebrospinal fluid pressure at once fell from 150 mm. water to zero. This fall was accompanied by a steady rise of arterial pressure. 35 c.cm. of a 10 per cent. solution of salt per rectum was followed in an hour by a fall of pressure from 144 mm. to 44 mm. below zero. 50 c.cm. of 30 per cent. solution per rectum were as effective as by mouth, and larger doses were not more potent. The lowered pressure continued for as long as eight hours in some instances. The administration of hypertonic solutions to animals the day before operation showed that the pressure had fallen under these conditions, for on the subsequent introduction of the manometer the initial pressure was found to be below normal. Glucose solutions produced similar but less pronounced results. Hypotonic solutions were not so striking in their effects, but produced a transient rise of about 45 mm. in the manometer. The changes in brain volume observed by Weed and McKibben were also seen. It is clear that the fall in pressure recorded is due in part to enlargement of the subarachnoid spaces by shrinkage of the brain, but this seems not to account for the total fall, and there is evidence that the normal relation between cerebrospinal fluid secretion and absorption is altered by these procedures.

In a short paper read before the Boston Society of Neurology and Psychiatry, Foley gave a brief account of further researches on this subject, in which the clinical application of the work is emphasized. By occipito-atlantoid puncture a manometer is connected with the subarachnoid space in animals, and filled with a solution containing iron ammonium citrate and potassium ferrocyanide. Following doses of hypertonic salt solution, a fall in pressure is observed and the solution in the manometer passes into the subarachnoid space. The later precipitation of Prussian blue (cf. *Medical Science*, 1920–1, **3**, 161) demonstrated that this solution had reached not only the subarachnoid space, but also the ventricles and the perivascular spaces of the brain. The manometer was then connected with a rubber catheter, which was passed into the aqueduct of Sylvius and thus registered the pressure within the ventricular system. This also showed a marked fall after the administration of hypertonic salt solutions. It appears that the effect of these solutions is to increase the osmotic pressure in the brain, and to cause a retrograde passage of cerebrospinal fluid from subarachnoid space into perivascular spaces and thence into the brain capillaries.

The same results are obtained in the human subject. Pressure is measured by lumbar puncture and the use of a water manometer. Not only does pressure fall, but brain protrusions through bone defects in the skull are seen to collapse.

Sachs and Malone have given intravenous injections of 100 c.cm. of a 35 per cent. solution of salt without ill effects in man, and have observed the collapse of protruding brain beneath the scalp.

Ebaugh and Stevenson investigated the case of an epileptic who had a bone defect in the left subtemporal region, the result of an exploratory craniectomy. They found that before and during minor and major epileptic fits there was a rise in intracranial tension, which ran roughly parallel with rise of cerebrospinal fluid pressure as determined by lumbar puncture. After administration of 4,000 c.cm. of a hypertonic salt solution by mouth, there was a fall of intracranial and of cerebrospinal fluid pressure. Conversely, water and hypotonic solutions caused a rise of both.

The full clinical usefulness of these observations has yet to be investigated, but it seems clear that they may be of use in dealing with cerebral fungation after craniectomy, and in preparing a patient with increased intracranial pressure for operative procedure. There are other possibilities, also, which it would be premature to discuss, and presumably the whole question is being explored in the Harvard Medical School Laboratory for Surgical Research, from which so much interesting and valuable work has come during the past few years.

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## THE BIOCHEMISTRY OF ECLAMPSIA

Recent work on eclampsia and the allied toxaemias of pregnancy may be conveniently summarized under three main divisions. We have in the first place, as in the modern literature of most diseases, observations on the rôle of acidosis in the aetiology of the condition; secondly, we have a considerable number of observations on renal and hepatic function in these disorders, and lastly certain miscellaneous observations, many of which bear on the conception of a primary thrombosis in various organs as the cause of the disease.

**Acidosis.** Work on acidosis, as the cause of the toxaemias of pregnancy, dates back to the investigations of Langemeister in 1903 on the alkalinity of the blood of pregnant women, and to the theory of Zweifel, that eclampsia is an intoxication due to over-production of lactic acid by the foetus. The very detailed observations of Hasselbach and Gammeltoft, who studied ten normal pregnant women, led to the conclusion that in normal pregnancy a slight acidosis is present. They found that during the course of pregnancy the ammonia coefficient of the urine rose steadily, and that this rise was accompanied by a corresponding fall in the alveolar $CO_2$ tension.

The introduction by van Slyke of a simple and rapid method of determining the alkaline reserve of the blood has led to further research on this point. Slemons finds that the $CO_2$ combining power of the plasma in normal pregnancies amounts to 37 to 50·4 c.cm. per 100 c.cm. of plasma, as compared with a figure of 55 to 75 c.cm. in healthy non-pregnants. Emge, who did not take the precaution of drawing the blood under oil, gives 31 to 59 c.cm. for the normal pregnant, the majority of the readings obtained lying between 42 and 52 c.cm. He states that an addition of about 5 c.cm. should be made owing to the method employed. In nine normal primigravidae studied by Losee, the plasma $CO_2$ content ranged from 49 to 56 c.cm.; and Losee and van Slyke, in 14 normal cases, found invariably figures below the average normal, and in 10 cases figures below the minimum normal of 55 c.cm. Results obtained by this method, therefore, show a definite reduction in the alkaline reserve of the plasma in uncomplicated pregnancies, and corroborate the statement of Hasselbach and Gammeltoft that in pregnant women a slight acidosis is normally present.

In eclampsia, pre-eclampsia, and the nephritic toxaemia of pregnancy there is, according to Slemons, no great reduction in the $CO_2$ combining power of the plasma as compared with normal pregnancy. Losee and van Slyke in their series of eclampsias found no case in which the $CO_2$ combining power of the plasma fell as low as 30 c.cm. per 100 c.cm. of plasma—'the figure at which in diabetics symptoms of distress begin to appear.' Losee in a further series confirms this finding, and concludes that the plasma $CO_2$ values in eclampsia and pre-eclampsia are practically identical with those of normal pregnancy, and are not indicative of a grave acidosis. Emge, in 17 cases of eclampsia and the allied toxaemias, observed values for the plasma $CO_2$ well within the normal limits for pregnancy. The few cases of pernicious vomiting, in which estimations of the plasma $CO_2$ have been made, show similar results. Emge, in four rather doubtful cases, found no definite or constant fall in the alkaline reserve, and Losee, in two cases with high ammonia coefficients, noted values of 38 c.cm. and 56 c.cm. for the plasma $CO_2$.

If, however, the ammonia coefficient is taken as the indication of the presence of an acidosis in pernicious vomiting, a very different picture presents itself. Losee, in the two cases quoted above, found 22 per cent. and 36 per cent. of the urinary nitrogen present as ammonia, and similar figures are given for three cases studied by Losee and van Slyke. These authors remark that 'it is noteworthy that, though cases of pernicious vomiting show strikingly high ammonia figures, the plasma bicarbonate indicates no greater degree of acidosis than may be observed in non-toxic cases'.

Gilliatt and Kennaway report two cases of pernicious vomiting in which abortion had to be induced, and was followed by rapid improvement. In both of these the ammonia coefficient was very high—the maximum reached being 46 per cent. of the total urinary nitrogen. The titratable acidity of the urine was also raised, and considerable amounts of acetone were excreted. In a third case, six months pregnant, the ammonia nitrogen was low and the excretion of acetone bodies small. In this patient, however, the diagnosis appears to have been doubtful, since perigastric adhesions and visible epigastric peristalsis were present. The authors discuss very fully the cause of the high ammonia coefficient in pernicious vomiting of pregnancy, and its relationship to the condition of inanition produced by the vomiting. They conclude from a study of the observations on fasting individuals, recorded in the literature, that the changes in the ammonia coefficient in pernicious vomiting are too marked and develop too rapidly to be due to the starvation alone. In explanation of the rise in the ammonia coefficient without corresponding depletion of the alkaline reserve of the plasma, they cite the experiments of Munzer on the administration of hydrochloric acid to normal men. In these experiments a rise in the urinary ammonia followed the administration of the acid, without appreciable fall in the $CO_2$ carrying power of the blood. They regard the ammonia as the first line of defence against acid introduced into the organism.

Cullis has had under observation a remarkable case of vomiting during pregnancy, in which, when first seen, the urinary ammonia reached the extraordinary figure of 77·9 per cent. of the total urinary nitrogen. On a high protein diet the ammonia fell rapidly, but never dropped below 9·8 per cent. throughout the pregnancy, which went to term.

In the toxaemias of the later months of pregnancy, Losee and van Slyke find no very marked rise in the ammonia coefficient. In Losee's series of cases none showed an ammonia percentage higher than 14·5. The older work of Wolf and Ewing shows figures very similar to these, and it would appear that the comparatively small increase in the ammonia coefficient noted in eclampsia and the pre-eclamptic state may fairly be attributed to the small food intake of such patients, and the effects of the muscular exertion involved in the fits.

White, using the methods of Sellards, has tested the sodium bicarbonate tolerance of normal and toxaemic cases. He finds that larger amounts of sodium bicarbonate are needed to produce an alkaline urine in toxaemic cases than in uncomplicated pregnancy. Normal cases required, on an average, 6·8 gm. of sodium bicarbonate to convert the urine to an alkaline reaction, toxaemic cases 45·3 gm., one fatal case showing a tolerance of no less than 120 gm. In this connexion, it may be noted that Palmer and van Slyke have found that Sellard's test gives no very definite indication of the degree of acidosis present in pathological cases. They determined the level of the $CO_2$ combining power of the plasma at which the urine became alkaline, and found that in disease this level might be greatly raised. In one instance enough bicarbonate was retained by a diabetic to raise the plasma $CO_2$ to 104·5 volumes per cent., without producing an alkaline urine. They conclude that when the bicarbonate test shows no acidosis none is present, but that, when an acidosis is indicated, the alarm may be false, or the condition greatly exaggerated. It would appear from the work of Palmer, Salvesen, and Jackson that the first depression of urinary acidity is a more reliable guide in estimating the degree of depletion of the alkaline reserve, as this occurs at a more constant level of plasma $CO_2$ combining power than the appearance of a definitely alkaline urine.

Recent work, therefore, does not suggest that an acidosis is the underlying cause of the toxaemias of the later months of pregnancy, any diminution in the alkaline reserve of the plasma that occurs being slight and inconstant, and the ammonia coefficient showing no great rise.

**Renal and hepatic function.** The normal level of the blood urea in pregnancy is disputed. Folin, working on a material of 100 cases, states that in healthy pregnant women the blood urea is abnormally low. He finds that the amount present varies from 5 to 9 mgm. of urea nitrogen per 100 c.cm. of blood—that is, 11 to 19 mgm. of urea, as compared with 11 to 12 mgm. of urea nitrogen in the non-pregnant. The total non-protein nitrogen of the blood is not diminished, but the urea nitrogen forms a smaller proportion of the total non-protein nitrogen than normally. This statement is traversed by Losee, who finds that the blood urea in pregnancy is at a normal level. Slemons, without mentioning the number of cases examined, gives 8 to 13 mgm. of urea nitrogen, as a standard figure for pregnancy, constituting 40 to 50 per cent. of the total non-protein nitrogen of the blood. Though in eclampsia the urea nitrogen may, according to his findings, rise to 50 or 70 per cent. of the total non-protein nitrogen, he does not believe that this ratio is of any value in predicting the outcome of a toxaemia. Folin, in explanation of the low figure for urea found by him, suggests that the kidneys in pregnancy are abnormally sensitive to waste products and that as a result the blood urea is reduced, while the total non-protein nitrogen is kept at a normal figure owing to the presence of excess of amino-acids retained in the circulation for foetal nutrition. This suggestion of an excess of amino-acids in the blood in pregnancy is, however, not borne out by the work of Losee and van Slyke.

In cases of eclampsia studied by Losee, no very marked rise in the urea nitrogen of the blood was present, the highest level reached being 31 mgm. per 100 c.cm. in a pre-eclamptic with a systolic blood-pressure of 238 mm. Hg. In his eclamptics the blood-urea nitrogen varied from 13 to 23 mgm. Working with van Slyke, the same author had previously found, in a series of eclamptics, figures varying from 25 to 46 mgm. for the non-protein, and 10 to 26 for the urea nitrogen of the blood. Slemons, from a material of 23 cases of eclampsia, pre-eclampsia, and nephritic toxaemia, concludes that the blood urea is increased to a greater or less extent in eclampsia, that the amount of increase is of no prognostic value, and that the blood urea does not differentiate eclampsia from nephritic toxaemia. In cases in which the uric acid content of the blood was examined, no definite increase was found. Losee has found no increase in the creatinin content of the blood in the toxaemias. Mackenzie Wallis noted blood ureas in eclampsia varying from 20 to 60 mgm., while in nephritis of pregnancy figures as high as 480 mgm. per 100 c.cm. were found and were not necessarily fatal. The same author has employed the urea concentration test of MacLean and de Wesselow in 9 cases, one eclamptic and the remainder nephritics. In all cases a low concentration power was present, indicating a severe renal lesion. In eclampsia, therefore, the increase in the non-protein nitrogenous constituents of the blood, if present at all, does not approach that seen in acute or chronic renal disease unassociated with pregnancy. Losee, in fact, believes that the low non-protein nitrogen of the blood should serve to distinguish true eclampsia from uraemia complicating pregnancy.

The diastase content of the urine in the toxaemias of pregnancy is dealt with by Mackenzie Wallis. He finds in normal pregnancy a diastase content of 10 to 33 units, the figure usually given for non-pregnant urines. In toxaemias of pregnancy the diastase content is, according to this author, abnormally high, reaching 200 units, and this is the only disease, apart from pancreatic lesions, in which such values are present. No other evidence of pancreatic lesion was, however, found. In neurotic vomiting no rise of the diastase content occurs. In contrast to the true toxaemias, cases of chronic nephritis complicating pregnancy show no increase in the urinary diastase, but rather a fall, and he believes that this may be a useful test for distinguishing the two conditions.

Fuhr, studying the renal lesions in eclampsia, finds the characteristic lesion to be swelling and thickening of the capillary walls of the glomeruli with similar but less constant changes in the vas afferens.

The importance of the liver in pregnancy is suggested by the work of Herring on the changes in weight of various organs in gravid albino rats. The liver gains 27·5 per cent. in weight, and the suprarenals 12 per cent., the thymus, pituitary, and thyroids show a very definite loss, while the kidney weight remains practically constant.

Our methods of estimating the functional capacity of the liver are, however, unsatisfactory, and little progress has been made in this direction in the study of the toxaemias of pregnancy. Since the original work of Wolf and Ewing, several attempts have been made to demonstrate the impairment of liver function in this group of diseases by determinations of the distribution of urinary nitrogen, a diminution in the percentage of nitrogen excreted as urea being accepted as evidence of hepatic failure. Since Folin's demonstration in 1905 of the effect of a low nitrogenous intake in reducing the percentage of the total urinary nitrogen, which appears as urea, the value of this method of determining the liver function has become less certain, and complete 24-hour collections of the urine, which are usually difficult to obtain in these cases, become essential. Losee and van Slyke state that the urea percentage of the total nitrogen in eclamptic urines is below the normal, the only urines of eclamptics showing more than 70 per cent. of the nitrogen in the form of urea being those obtained one or more days *post partum.* They find urea nitrogen percentages as low as 46, with undetermined nitrogen—that is to say, the remainder nitrogen after deduction of urea, ammonia and amino-nitrogen—correspondingly high. They were unable to demonstrate any rise in the amino-nitrogen of the blood or urine, as compared with normal pregnancies, and conclude that there is no evidence of impairment of the desaminating function of the liver. They suggest that the urinary nitrogen distribution resembles that found by Nencki and Pawlow in the urine of dogs after extirpation of the liver. Losee in his later paper gives similar figures.

Several authors have made determinations of the blood-sugar in these disorders, probably with a view to obtaining evidence of a deranged carbohydrate metabolism due to impairment of liver function. Losee finds normal values. Slemons states that after convulsive seizures hyperglycaemia may be present, but that it is admittedly due to the convulsions. The latter author also finds that hyperglycaemia may be present in nephritic toxaemias with raised arterial tension. Mackenzie Wallis has never seen hyperglycaemia in the toxaemias of pregnancy.

The estimation of urinary glycuronic acid by a colorimetric method, based on the reaction of this body with naphtho-resorcin (originally described by Tollens), has recently been revived in France as a test of liver function. The test is either made on a normal specimen of urine, or the urine is examined after a provocative dose of camphor. A dose of 0·5 gm. of camphor produces a marked excretion of glycuronic acid in the normal individual, but in cases of hepatic disease this reaction may be absent. Chiray, who has utilized this test, states that there is a marked diminution in the excretion of glycuronates in cases of vomiting in pregnancy. He quotes Jean and Roger as finding that in cases of pregnancy, complicated by oedema and albuminuria, glycuronic acid may disappear from the urine. These authors regard the disappearance of glycuronic acid as definite evidence of failure of hepatic function in such patients.

To sum up, recent biochemical work on the impairment of renal and hepatic function in the toxaemias of pregnancy has not added materially to our knowledge. We cannot, in fact, at present state definitely whether the toxaemias of the later months of pregnancy are manifestations of a single disease, or whether several distinct pathological entities are included under this head. Though some authors appear to draw a distinction between pre-eclampsia and nephritic toxaemia, the terminology is not apparently correlated with any observed chemical data, nor is it apparent that the different names employed correspond to distinct clinical phenomena.

Our methods of testing renal function have advanced considerably in recent years, but their application to eclampsia has not been fruitful. Deductions as to renal efficiency from the estimation of waste products in the blood are not likely to be satisfactory until we have more definite knowledge as to the concentrations in which these substances occur in normal pregnancies. The normal concentration of the most easily determined of these bodies—the blood urea—is still in dispute. The largest material examined, the 100 cases of Folin, suggests that the blood urea is at an abnormally low figure during pregnancy, but no satisfactory explanation has been given, nor are the figures given confirmed by the work of other authors. The only definite evidence of impairment of renal function in the toxaemias of pregnancies lies in the results given by the urea concentration test, but only a very few cases have been examined from this standpoint.

It is useless to pretend that we possess at present any satisfactory method of estimating the functional capacity of the liver. No definite advance in this direction has been made since the subject was investigated by Rowntree, Chesney, and Marshall, whose paper well illustrates the unsatisfactory condition of affairs in this field of medicine. That an abnormal urinary nitrogen distribution is present in the urine of many of these cases, when compared with that seen in the urine of healthy non-pregnant individuals on a full protein diet, appears to be proved. The interpretation of this fact is the difficulty. Data of the urinary nitrogen distribution in healthy pregnant women are scanty. Losee, who has examined nine normal primiparae in the ninth month of pregnancy, gives urea nitrogen percentages varying from 71 to 91·7 per cent. The very marked diuresis present in all his cases suggests that the 24-hour figures were calculated from 72 minute samples collected for the calculation of an Ambard index of renal efficiency. If this is the case, such urines can hardly be considered as fair samples, since a diuresis is known to produce excessive temporary urea elimination. On the majority of recorded cases of eclampsia, the figures of nitrogen distribution are calculated from samples, since in the nature of the case 24-hour urinary collections are an impossibility. That under conditions of low nitrogen metabolism extremely low percentages of urea nitrogen are found, even in absolutely healthy individuals, was shown long ago by Folin: such conditions must usually be present in eclamptics, and low nitrogen percentages cannot therefore be accepted as evidence of hepatic failure unless the total nitrogen metabolism can be measured. The extraordinary persistence of the urea-forming function of the surviving liver, in spite of the action of such poisons as phosphorus, is well illustrated by recent work of Löffler. It cannot be said that the numerous efforts to demonstrate hepatic failure by the study of the urinary nitrogen distribution have led to any striking results, and it does not appear that any satisfactory clinical test will be evolved along these lines. Of failure of the desaminating function of the liver in these disorders Losee and van Slyke could obtain no evidence, and further work on the glycuronate test appears to be necessary before its value can be taken as proved.

**Miscellaneous Observations.** Bela Váró, of the University of Buda Pesth, working on a considerable material, reports a fall in the number of eclamptic cases during the war years. This fall was more marked in Germany than in Austria, a fact which the author correlates with the more marked under-nutrition of the German population. In Hungary he found that the percentage incidence and mortality remained unaltered during the war among the classes which were able to maintain their standard of nutrition. In his eclamptic cases the mortality fell from 24 per cent. before the war to 14 per cent. during the war years. Gessner notes a steady fall in the Baden statistics of eclampsia from 1915 to 1918 inclusive. He points out that two possible factors are involved, the undernourishment of the population, and the employment of women in industrial occupations, almost up to the time of their confinement. Numerous German authorities are quoted by Bela Varo in support of his statement that the eclampsia rate fell during the war.

Kehrer has examined the calcium content of the blood in the toxaemias of pregnancy. In Dresden the calcium content of the blood of healthy women was found to be 7 to 7·3 mgm. per 100 c.cm. No diminution occurs during the first half of pregnancy, but during the later months the amount present falls to 6·5 to 6·6 mgm., and remains at this low figure during the puerperium. In eclampsia the fall is more marked, and the blood calcium only amounts to 5·4 to 5·8 mgm. per 100 c.cm.

Denecke has estimated the blood-platelets in five cases of eclampsia and finds a marked diminution in these bodies, as compared with the normal or increased count in healthy pregnancies. The platelets remained at a low level for at least five days after the termination of the fits. The author regards the fall as a symptomatic thrombo-penia, due to inclusion of the platelets in thrombi formed in the course of the disease.

Abderhalden, working on the rate of sedimentation of red cells, finds that substances are present in the plasma of pregnant women which accelerate sedimentation. Blood corpuscles of normal persons sediment quickly in the plasma of pregnant women, while corpuscles from the pregnant sediment slowly in normal plasma. The accelerating substance is dialysable. The same phenomenon has been studied by Linzenmeier, who states that it is inconstant during the first half of pregnancy, but that it is marked during the later months and for the first eight days after labour. He believes that it is of value as a diagnostic point in the differentiation of pregnancy from myoma. Starlinger, who has recently examined the velocity of sedimentation of the red corpuscles in pregnant and other bloods, finds that the rate of settling bears a definite relationship to the fibrinogen content of the plasma, a high percentage of fibrinogen producing a rapid sedimentation. The fibrinogen content of the plasma was determined by the refractometer. Defibrination of the blood with glass beads led to an extraordinary delay in sedimentation. Rapid settling is associated with clumping of the red corpuscles, and the author explained the phenomena observed on the lines of the theory of Herzfeld and Klinger, who believe that the stability of colloidal protein solutions is due to adsorption by the protein molecule of water-soluble polypeptids. If Starlinger is correct in his belief that fibrinogen is the accelerating substance, his conclusions directly conflict with the work of Abderhalden, who finds that the accelerating body is dialysable.

Dienst, in a lengthy article without many experimental data, reiterates his belief that the underlying cause of eclampsia is thrombus formation, associated with a raised content of the blood in fibrinogen and fibrin ferment. He states that hirudin is of value as a therapeutic agent. The blood of eclamptic women contains no antithrombin, nor was this substance present in eclamptic livers. In normal pregnancies the blood antithrombin is increased. He gives figures showing the marked fibrinogen rise in normal pregnancy, and the abnormally high levels reached in eclampsia and nephritis gravidarum. By injecting homologous fibrinogen intravenously into rabbits, lesions suggesting those found in eclampsia were produced. It is, however, known that in infections complicating pregnancy the fibrinogen content of the blood may rise to at least as high levels as are seen in eclampsia without producing symptoms. Fibrinogen excess cannot therefore be the sole cause.

Young and Miller, from a study of 40 cases of eclampsia and pre-eclamptic toxaemias, conclude that the condition is due to the absorption of toxic products formed early in the degeneration of portions of the placenta, the blood-supply of which has been interfered with. Placental infarction may be due to traumatic detachment from the uterine wall, or more often to thrombosis. Absorption of the toxic products can only occur if part of the placenta remains attached to the uterine wall, and toxaemia is therefore conspicuous in concealed accidental haemorrhage, and may occur in placenta praevia. They find support for their theory of the toxicity of placental degeneration products in the observations of Quénu and Delbet on the rôle of early disintegration products of muscle in the causation of wound shock. The phenomena of eclampsia, however, especially the very marked rise in the blood-pressure, are so different from those of wound shock that the analogy would appear doubtful. In explanation of post-partum eclampsia the authors cite the delayed action of such poisons as chloroform and phosphorus. They accept the presence of a trace of protein in the urine as definite evidence of a toxaemic condition, a supposition which would appear to require further proof, especially since it has been shown by Beer that fatal eclampsia may occur without albuminuria. Slight albuminuria is not unusual in labour, and it seems more reasonable to attribute its appearance to the muscular exertion involved, rather than to invoke as its cause a toxaemic state.

Haffner has worked out the incidence of albuminuria and placental infarcts in a material of 400 consecutive cases. The placentae were carefully examined and thoroughly sliced, and several examinations of the urine were made on each patient. In 73 cases albuminuria was detected, and of these 44·2 per cent. showed no placental infarction; of 185 placentae which showed infarction, 77 per cent. came from the women in whose urine no albumin had been detected. In 30 per cent. of these placentae the infarctions were recent. He concludes that there is no direct relationship between albuminuria and placental infarction.

Zweifel summarizes the theories which have from time to time been advanced to explain eclampsia. They number 15. In his own work he has repeated the experiments of Grafenburg, Lockemann, and Thiess. These authors, who regarded eclampsia as an anaphylactic phenomenon, had experimented on the injection of foetal serum into pregnant and non-pregnant animals. They came to the conclusion that the non-pregnant animal could be sensitized to the serum of the foetus of the same species—that, in short, the foetal proteins behaved as foreign proteins. The injection of foetal serum into the pregnant animal was frequently fatal. Zweifel has repeated the experiments, but with absolutely negative results. Working with rabbits and guinea-pigs, he found that foetal serum, and serum from the placental blood, did not sensitize the animals of the same species. He gives various reasons for not regarding eclampsia as an anaphylactic phenomenon, such as its non-occurrence in guinea-pigs, the unfavourable conditions for its production in pregnancy, where the mother is constantly exposed to the foetal protein and should rather pass into an anti-anaphylactic state, and its comparative rarity in the human being. An excellent bibliography of the subject is appended to his article.

It is, of course, impossible to discuss here the numerous theories of eclampsia, but it may be pointed out that none of the suggestions hitherto propounded have met with any general acceptance. If we define acidosis as a lowering of the alkaline reserve of the plasma, the acidosis encountered in the toxaemias of the later months of pregnancy is not markedly, if at all, in excess of that found in normal pregnants. The significance of the raised ammonia index and excretion of acetone bodies found in pernicious vomiting is still in dispute, and the belief that they are the signs of a causative acidosis, rather than purely inanition phenomena, is not based on any very convincing evidence. Attempts to demonstrate failure of hepatic and renal functions, correlated with the pathological lesions found *post mortem* in these organs, have on the whole failed. Of the respective parts played by the liver and kidneys in the disease we have but little knowledge. The fact that albuminuria may be absent in eclampsia, and the absence of evidence of any marked retention of waste products in the blood, suggest that the kidney lesion is probably secondary. Post-mortem evidence shows that the hepatic lesion is more constant, and that it may undoubtedly precede the fits, but we have as yet no method of following changes in the hepatic function. As to the initial cause of the damage to liver and kidney we are in complete ignorance. The various suggestions, summarized in the last section (over-nutrition, calcium deficiency, fibrinogen and fibrin ferment excess with resulting thrombosis, absorption of toxic products from the placenta, and anaphylaxis due to introduction of foetal protein), though interesting in themselves, are in no case based on such incontrovertible evidence as to offer a firm foundation for rational treatment and prophylaxis. Eclampsia still remains 'die Krankheit der Theorien'.

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# ABSTRACTS

## NEUROLOGY

**Kaufman, I.** Über die Markbildung des Hinterstranges des Rückenmarks. [**The myelinization of the posterior column of the cord.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **67**, 190.

**Richter, H.** Zur Histogenese der Tabes. [**The essential lesion of tabes.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **67**, 1.

**Schaffer, K.** Bemerkungen zur Histopathologie der Tabes. [**Observations on the histopathology of tabes.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **67**, 222.

In this important series of papers from the laboratory of Professor Karl Schaffer are recorded and discussed a series of very significant conclusions on the origin and nature of the essential lesion of tabes.

The anatomical and pathological basis of these conclusions is provided by the observations of Kaufman on the mode of myelinization of the posterior roots and columns of the cord, which are then correlated with the pathological findings of Richter and Schaffer.

Kaufman does not agree with the views of Flechsig on the myelinization of the posterior columns, but her observations conform closely to those of O. Vogt on the myelinization of the cerebral hemisphere and with some observations of Brodman on the cord. Flechsig divided the posterior columns into four zones: anterior, middle, postero-mesial, and postero-lateral zones, each of which formed a territory with its own myelinization period. Kaufman finds that the posterior columns are myelinated later than the antero-lateral columns and the posterior roots later than the anterior roots. The posterior columns in a four-months' foetus are non-myelinated. Myelinization first appears in Flechsig's middle zone, which corresponds to the root-entry zone. From this it spreads slowly throughout the column, and the only differentiation permissible is into early and late myelinated areas. The former corresponds with the root-entry zone, the latter with the postero-mesial zone of Flechsig, or the area of Goll's column. The short and medium length fibres first gain their myelin sheaths, the long ascending fibres of the column do so later. Schaffer points out that the root-entry zone is particularly rich in posterior root fibres, and contains short, medium, and long fibres; indeed all the posterior root fibres of a given segment. Hence it is not surprising that myelinization should appear particularly rich here, and its intensity depends upon the early myelinization of short and medium fibres. Therefore, the short and long fibres of the columns differ not only topographically, but also biologically, as the myelinization processes indicate. Degeneration of posterior root fibres follows identical laws, the short and medium fibres which lie thick in the root-entry zone and never pass into the postero-mesial zone always degenerate earlier than the long fibres of the latter zone. Hence the distribution of the posterior column degeneration seen in tabes is by no means specific for this disease, cannot be described as selective, but depends upon the anatomical distribution and the biological characters of these two groups of fibres.

Richter, from the serial examination of the posterior roots of fourteen cases of pure tabes and ten of tabo-paralysis, finds that **the essential lesion of tabes** consists in a peculiar form of granulation tissue which develops primarily in the sheaths of the posterior roots, whence it spreads secondarily into the roots (peri-fascicular and then endo-fascicular spread), and causes them to degenerate. The essential cell of this tissue is described as a fibroblast, which develops in the endothelial lining of the lymph channels and in the connective tissue spaces of the arachnoid and dural sheaths. The granulation tissue thus formed tends, like granulation tissues in general, to become sclerotic ultimately. The nerve degeneration secondarily produced is focal and of irregular distribution and intensity. Thus some roots are but slightly degenerated, others completely. Nor is the process at all symmetrical. Commonly, the short and medium fibres of the roots are the first to suffer, and upon this fact depends the distribution of the purely secondary posterior column degeneration. In pure cases no other lesion is found, nor is there any meningitis in the common sense of the term. No lymphocytes or plasma cells are found in the lesion, except in cases of tabo-paralysis, where they are found in addition to the lesion already described. Spirochaetes are of common occurrence in this essential tabetic lesion, and hence its syphilitic origin is clear. The lesion may be found in all grades of development, intensity, and extent in cases of tabes.

These findings, as Schaffer points out, are directly against the view that the essential lesion of the disease is a primary selective degeneration of certain fibres in the posterior columns. They point to the fact that the nerve lesion is secondary, and depends for its prolongation into the cord and its distribution there to well-established anatomical facts. Tabes, therefore, depends upon the local presence and growth of spirochaetes in the sheaths of the posterior roots and upon the chronic granuloma resulting from their action on the tissues, the nervous lesion being purely secondary.

These papers are very lengthy and occupy over two hundred pages of the journal. An adequate abstract is, therefore, not easy within a short compass, and the papers should be consulted in the original by those interested. That they are of great importance is clear.

F. M. R. W.

**Spiller, W. G. The treatment of spastic gait by permanent flexion of the great toe.** *Arch. Neurol. & Psychiat.*, 1921, **5**, 771.

It is said that as far back as the days of Charcot the infirmières of the Saltpetrière knew that the extreme extensor rigidity of the lower limbs in some cases of spastic paralysis could be readily and easily overcome by the simple expedient of forcible plantar-flexion of the toes. When this is done, the rigid limb draws up fully and powerfully, and the nursing and manipulation of the patient are facilitated. Thanks to Sherrington's experimental work and to its clinical application we know that we are employing the nociceptive flexion reflex of the limb when we stimulate the foot in this way, and that there is a wide range of stimuli applied to an extensive region of the limb which will give the same result.

Spiller proposes to make use of this fact to overcome the difficulty spastic patients experience through their inability, from combined weakness and extensor spasticity, to flex the legs. The toes are maintained in a position of plantar flexion by a suitable bandage or surgical boot. A case was demonstrated at a meeting of the Philadelphia Neurological Society, and the application of a roller bandage beneath the toes was followed by striking improvement in the patient's gait, flexion of the limb being greatly improved. Whether a permanent flexion reflex can be produced in this manner remains to be seen. F. M. R. W.

**SCHAFFER, K.** Über die intraspinale Bifurkation der Hinterwurzelfasern beim Menschen. [**The intramedullary bifurcation of the posterior root fibres in man.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **67**, 215.

A bifurcation of the entering posterior root fibres is the rule in man. It is to be seen in the root-entry zone. The bifurcation is commonly wide-angled, and the ascending and descending processes are usually about equal in thickness. Occasionally 'trifurcation' is seen. A small 'plasmabrucke' or web unites the diverging processes at their origin.

F. M. R. W.

**DANDY, W. E. The diagnosis and treatment of hydrocephalus due to occlusion of the foramina of Magendie and Luschka.** *Surg. Gynec. & Obst.*, 1921, **32**, 112.

Every case of hydrocephalus has a specific cause, the old conception of an 'idiopathic' variety being now practically abandoned. Dandy discusses the ancient controversy as to the presence or absence of the foramina of Magendie and of Luschka. The presence of these foramina is essential for the escape of cerebrospinal fluid from the intra-ventricular system into the subarachnoid space, whence it is absorbed. Conversely, closure of one or more of these three openings will lead to an embarrassed fluid escape and consequent hydrocephalus unless the remaining openings or opening are sufficient in size to compensate for the occluded channel. Dandy has previously explained other varieties of hydrocephalus; in the present paper he confines himself to that resulting from closure of the three medullary foramina. Of this closure there appears to be two types, one intra-uterine with hydrocephalus present at birth and due probably to failure of the foramina to develop, the other occurring at any age, but always following meningitis. The roof of the fourth ventricle may be found enormously distended in such cases, the vermis suppressed, and the cerebellar hemispheres widely separated. If indian ink is injected into the spinal theca at autopsy it may be found to have spread up over both hemispheres, but will not enter the distended ventricular system. The clinical diagnosis is made by injections into the ventricle of either air with subsequent radiography, or of indigo-carmine or phenolsulphonephthalein and examination of the thecae, cerebrospinal fluid, and of the urine. Dandy describes two adult cases in which the diagnosis was tumour of the posterior fossa, and at operation sealing of the basal foramina was found. Without a history of antecedent meningitis there can be little certainty of diagnosis before operation. The operative treatment of occlusion of the foramina of Magendie and of Luschka consists in the exposure of the cerebellum as for a posterior fossa tumour. The scarring about the foramen of Magendie should be excised, or, if there is a bulge at one side of it, a new foramen may be cut in this. In the two adults recovery followed operation; in the child the condition was so advanced that death followed puncture. Apparently no similar cases have come to operation, so that these cases are unique from a therapeutic point of view. G. J.

**Byrne, J. Paradoxical pupil dilatation following lesions of the afferent paths.** *Am. J. Physiol.*, 1921, **56**, 113.

After avulsion of one superior cervical ganglion or section of one sympathetic nerve the pupil on the side of the operation shows an increased instability and responds more readily to dilator stimuli than its fellow on the normal side. This is supposed to be due to the interruption of afferent impulses by way of the cervical sympathetic. Since it is known that stimulation of sensory nerves produces pupil dilatation, the author tested for the occurrence of paradoxical effects following upon lesions of the afferent pathways. It was found that after section or injury of one sciatic nerve paradoxical phenomena can be elicited in the pupil of the contralateral side, which reach a maximum after about 14 or 15 days and then disappear again.

The conclusion is reached that in the waking state afferent impulses from the periphery impinge upon the motor neurones situated in the lateral horns of the upper thoracic segments (lower cilio-spinal centre of Budge) and condition reflexly the outflow of impulses which reach the pupil dilator mechanism *via* the cervical sympathetic. W. C.

## PATHOLOGY AND BACTERIOLOGY

**Bordet, J.** Considérations sur les théories de la coagulation du sang. [**Considerations on the theories of blood coagulation.**] *Ann. de l'Inst. Pasteur*, 1920, **34**, 561.

This is an elaborate memoir presented by Jules Bordet on the occasion of the jubilee of Metchnikoff. While it is not intended to be a treatise on the coagulation of the blood, it contains the author's well-considered views on a subject to which he has added a great deal of knowledge.

Although the phenomenon of blood coagulation lends itself admirably to investigation, since it occurs *in vitro*, its secret has not yet been completely revealed, in spite of innumerable experiments. It is helpful to give at intervals an outline of the work that has been done to co-ordinate the various views brought forward. Only the essential facts are, however, here recalled.

The coagulation of blood consists in the organization (in the form of fibrinous strands) of colloidal particles of fibrinogen, which as Fredericq showed in 1877, pre-exists in the circulating plasma. *In vivo*, plasma is a stable colloidal medium whose constituents are in the dispersed state; when bleeding occurs the first determining influence which initiates the series of phenomena that results in the separating out in the solid form of fibrinogen is often its admixture with the juices of the wound which contain some active elements. In this case there is a superadded factor, and we shall preferably consider here the coagulation of pure blood that is without the influence of any external substance; an essential influence bringing about coagulation is contact with a foreign body such as glass. Here the glass acts by virtue of its physical contact with the blood and not on account of its liberation of any soluble substance. This contact, an external factor, lets loose certain properties possessed by the blood itself, and it is in this way that the direct coagulating principle, the fibrin ferment, or thrombin, is formed, as is found in the serum issuing from a clot. Schmidt has shown that the thrombin does not reveal itself, at any rate in perceptible amounts, in the fluid plasma. Taking, therefore, the phenomenon of coagulation as a whole, one can distinguish many phases. But the principal problem is really that of the appearance of the thrombin, the rôle of the fibrinogen being purely passive. Fibrinogen can be extracted from the plasma in an approximately pure state. It is to be borne in mind that blood has a very complex composition, and that the physiologist investigates not the coagulation of fibrinogen in its pure state but enveloped within a definite environment.

The colloids of the blood are connected amongst themselves by the bonds of molecular affinity. Blood possesses a well-defined osmotic pressure; it contains alkaline salts, and, further, the influence of the osmotic pressure or the reaction upon the production of thrombin is obvious. On the other hand, the fibrinogen which one endeavours to purify is found to be more soluble in the presence of traces of alkaline salts than in neutral solution of sodium chloride. There is thus reason to believe that certain colloids contribute to the maintenance of the dispersed state, whilst the other elements in suspension favour its aggregation into fibrin. All these influences must now be considered.

**Fundamental processes and factors in coagulation.** Since the blood of many laboratory animals coagulates quickly there is here an indication to retard the process at various stages in order to learn more about the different phases. Low temperatures retard coagulation. This has been made use of to separate the plasma by centrifugalization from the cells. This procedure, however, hardly lends itself to a deep analysis. The raising of osmotic pressure by adding to blood, on its escape from the blood-vessels, sufficient quantities of salts such as magnesium sulphate or sodium chloride, prevents coagulation (Hewson, Schmidt); such saline plasmas have been of great service in the investigations.

Plasma obtained in this way, especially by centrifugalization and addition of 3–5 per cent. sodium chloride, has afforded excellent results. By subsequent dilution of plasma so treated with distilled water coagulation occurs spontaneously and can be effectively studied. The discovery of Arthus and Pages, that the calcium ion was essential to coagulation, had a decisive influence. The addition to blood as it issued from the vessels of precipitants of calcium, such as sodium oxalate, sodium fluoride, sodium citrate, takes away its power of coagulating spontaneously. The subsequent addition of calcium chloride restores this property. Coagulation can also be prevented by agitation with movable bodies. Blood received into a vessel whose inner surface is smeared with oil or vaseline coagulates but slowly (Freund). Bordet and Gengou have reported that by centrifugalization in paraffin tubes they succeeded in keeping the blood of a rabbit in a fluid condition for over 24 hours. This blood immediately coagulated on being transferred to an ordinary tube. Delezenne has shown that the blood of birds coagulated exceedingly slowly if all foreign bodies, especially débris from the wound, were prevented from gaining access to it. Thus in all observations on coagulation it is necessary to take the precaution in the collecting of the blood to prevent all access of foreign elements. The blood-cells, and especially the blood-platelets, are well preserved if the blood is collected in an oxalate medium, as was shown by Pringle and Tait, Aynaud, and others. Contact with a rough surface and the presence of soluble calcium salts are factors in coagulation and it suffices for the prevention of the phenomenon to eliminate them. It is conceivable that the same result might be obtained by absorbing the thrombin or its precursors. Bordet and Gengou recognized this in their study of various chemically inert precipitants, notably barium sulphate and calcium fluoride. Blood collected in its exit from an artery when mixed with a small quantity of tricalcium phosphate remains fluid. Its centrifugalization gives a perfectly stable fluid plasma. All these facts are mentioned as the procedures indicated furnished means for obtaining fluid plasma which may be studied at leisure. Having succeeded thus in separating plasma from cells, one should attempt to go farther by considering the cellular element as well as the plasma. The blood-platelets can be separated from the corpuscles by utilizing the fact that they are relatively very light, especially in mammals.

By centrifugalizing oxalated blood at a moderate speed it is found that the plasma contains only the platelets. The plasma is decanted off and centrifugalized for a prolonged period at high speed. This results in the sedimentation of the platelets. These can be washed with slightly oxalated physiological saline (Mosen, 1893). It is important to be able to isolate the platelets, as they play a very important rôle in coagulation. As for the plasma, one of the means by which it is hoped to dissociate the various factors contributing to the bringing about of coagulation was that of heating to graduated temperatures. Fibrinogen is precipitated at 56° in the form of flakes which do not redissolve on cooling. It follows, therefore, that the fluid plasma remaining after such treatment is no longer coagulable. Unfortunately, thrombin, at any rate in its plasma or serum environment, is also affected by temperature, as is also one of its precursors (prothrombin). Heat, therefore, has not been of much use in this respect; on the other hand, concentrated sodium chloride solution has proved invaluable. Fibrinogen is completely precipitated by full saturation with sodium chloride, and is partially precipitated by half-saturation. By repeated precipitation and re-solution Hammarsten succeeded in obtaining a pure solution of fibrinogen in weak saline. But it does not remain in solution for any length of time. The product thus obtained is rendered more stable by the introduction of a trace of sodium carbonate (Nolf). Even under these conditions apparently spontaneous coagulation occurs after a certain time, and this has been attributed to the difficulty of avoiding the entrance into the solution either of thrombin or its precursor. But this may not be the true explanation.

One cannot dogmatically assert that thrombin is the sole agent capable of bringing about coagulation of fibrinogen. Gratia has recently shown that certain microbes possess this power. Arthus has shown, on the other hand, that the venom of certain snakes possesses more powerful coagulating properties. It may well be that coagulation is a property inherent in fibrinogen, and that it can manifest this property more easily when certain constituents of the plasma normally present are removed. On the other hand, there may be constituents of the plasma, other than thrombin, tending to separate out from it. These bodies are precipitated together with fibrinogen and render the latter unstable and impart to it the tendency to come down from its solution in a flocculent manner or to coagulate. The delicacy of the conditions of colloidal equilibrium is well known, as is also the fact that in a mixture of colloids certain constituents may either hasten or hinder by their presence the precipitation of others.

The conditions of coagulation of pure blood or a normal plasma on the one hand and an isolated solution of fibrinogen on the other are not identical. The inferences drawn from observation on the latter must be very carefully scrutinized. Thrombin is most certainly the essential factor in coagulation under normal conditions. It has been recognized that thrombin has the power of being adsorbed to fibrin. But fibrin is to be looked upon as a modified form of fibrinogen. According to various authors there is nothing to show that in the absence of thrombin this change would not take place even after its extraction from the plasma. Pekelharing was the first to demonstrate the method of extracting thrombin—saturation of oxalated plasma with sodium chloride and dissolving the precipitate of fibrinogen thus formed with slightly alkaline water. The solution thus obtained contains a principle which causes the coagulation of fibrinogen. When blood coagulates spontaneously the soluble fibrinogen is converted into soluble fibrin. Serum issues from this clot, and is found to contain thrombin. It is an active coagulant, but it must be here inquired whether serum possesses as powerful coagulating properties when it is incorporated in the plasma with its cells as it does when the plasma is devoid of the cellular elements. It has been known for a long time that the presence of the blood-cells favours coagulation and that the cells contribute to the formation of the coagulating principle.

Lesourd and Pagniez in 1909 emphasized the importance of the rôle played in this connexion by the platelets. Experimental evidence has fully confirmed this view. If the platelets are removed from blood it undergoes coagulation at an excessively slow rate. The coagulating power of thrombin is not only in proportion to its concentration but it also depends on its age. Bordet and Gengou have shown that its deterioration is very rapid. Schmidt long ago devised a process of purification of thrombin. He precipitated the serum by alcohol, dried the precipitate, and extracted the thrombin from it by water.

**Origin of thrombin and order of succession of phenomena.** Circulating blood, collected in a paraffined tube, or blood treated with strong solutions of sodium chloride, or oxalated blood, do not contain thrombin. The essential factors contributing to the formation of thrombin from its precursors (the osmotic pressure being favourable) are soluble calcium salts and contact with a solid body to which the fluid adheres. But if thrombin has once been formed by the presence of such factors it can then cause coagulation both in the absence of calcium salts and even in a paraffined tube, while, as regards strong saline, it counteracts the action of thrombin. In circulating blood or still fluid plasma thrombin is not completely formed, but exists in an inactive form, prothrombin, which in the presence of calcium salts and by contact produces active thrombin.

But, in 1903, Morawitz showed that serum becomes suddenly and considerably more active by introducing into it a little of the juice of the wound or an emulsion of the crushed tissues. This important fact was confirmed by Fuld and Spiro. And yet tissue juice does not show in itself coagulating energy towards oxalated plasma. Morawitz, Fuld, and Spiro deduced from this that besides thrombin the serum contained a certain quantity of unchanged prothrombin. The thrombin was formed by the mutual action of two generators, one (thrombogen) existing in plasma, the other (thrombokinase or cytozyme) existing as much in the tissue-cells as in the blood-cells. One gathers, therefore, that the addition of thrombokinase in the form of tissue juice brings about the transformation of the prothrombin which the serum contains in excess and thus causes an added quantity of thrombin to appear. Normally thrombokinase remains within the cells, but is freed when blood is withdrawn or the tissues are lacerated.

In this way is explained the fact that the addition of tissue juice to extracted blood markedly accelerates clotting. Morawitz reported that tissue juice loses much of this accelerating power when it is warmed to 58°.

Therefore, he supposes (erroneously, as we shall show) that the thrombokinase or cytozyme is a thermolabile substance, the other generator (thrombogen) being also very sensitive to heat. There is no doubt that the tissue-cells contain active substances which the blood does not. It must not be forgotten that tissue juice injected into the circulation is strongly toxic and can cause rapid death in an animal by the development of intravascular coagulation. On the other hand, there is nothing to show that the tissues on their part may not equally contain principles which exist in the blood-cells. This is really the case, and the idea of the existence of two generating substances is likewise confirmed when we study the coagulation of pure blood. We are justified in believing that both tissue juices and the blood-platelets contain thrombokinase.

Bordet and Delange called that component contained in the serum ‘ serozyme ’, and that furnished by the platelets ‘ cytozyme ’. Heated to 58° the serum loses its power to produce thrombin by the addition of platelets, while the latter heated to 100° still retain their thrombin-producing power. Thus serozyme is thermolabile and cytozyme is thermostable. Whether the platelets are fresh or warmed they equally accelerate the coagulation of diluted oxalated and recalcified plasma. On the other hand, the coagulating power of tissue juice to plasma is considerably weakened by heating to 58°, as was shown by Morawitz, but does not completely disappear, as Bordet and Delange have confirmed. Tissue juice, even when warmed to 100°, is still able to yield thrombin when added to serum. There is thus reason to believe that tissue juice, as well as platelets, contain cytozyme of thrombokinase—i. e. the thermostable generator of thrombin.

In addition, they contain a special generating substance much more sensitive to heat and of a protein nature, and which, not being traceable in the platelets, appears to be foreign to blood. To sum up, nature has added another factor of coagulation to those which blood already possesses. The tissues have a special constituent which accelerates this coagulating process when the blood comes into contact with it. The tissues also contain thrombokinase as does the blood. This idea was definitely stated by Bordet and Delange when they determined the chemical nature of thrombokinase. Wooldridge observed that the addition of lecithin brought about the coagulation of peptonized plasma. Schmidt and his pupils had recognized that certain substances extracted from the tissues by alcohol, and showing the solubility characters of lipoids, favoured the coagulation of plasma, and increased the coagulating power of serum. But the question was—how do these accelerating substances act? Do they favour the production of thrombin without entering into its composition, as Schmidt thought? Is one of the generators a lipoid? Do the lipoids facilitate the action of a preformed thrombin on fibrinogen? One cannot determine between these hypotheses without systematic experimentation.

Platelets rich in lipoidal cytozyme do not set free any trace of thrombin when they are allowed to macerate in physiological saline or distilled water, which they certainly would if they possessed the two generators of this principle. It is concluded that the other generator (cytozyme-thermolabile) does not come from blood-cells but from plasma. Oxalated plasma, to which is added a little suspension of tricalcium phosphate, which is afterwards eliminated by centrifugalization, no longer coagulates spontaneously by recalcification. It does not coagulate any better by addition of platelets, or tissue juice, or cytozyme extracted in lipoidal state, while it solidifies promptly by addition of thrombin. But if, going back to the phosphate sediment obtained from plasma by physiological solution, it is dissolved in carbonic acid, the solution so obtained, with cytozyme added, acts as energetically as thrombin (Bordet and Delange).

The expression ‘thrombin generator’ applied to serozyme and cytozyme implies that these react on each other. This fact is easily demonstrated by remembering that thrombin deteriorates rapidly. A remarkable fact is shown in the time which thrombin requires to appear when lipoidal cytozyme or platelets are mixed, on the one hand, with serum produced by the coagulation of recalcified oxalated plasma, on the other hand, with similarly oxalated plasma, but which has just been recalcified and so is not yet coagulated. In the mixture of cytozyme and serum, thrombin is produced at the end of a measurable but short time. In the cytozyme-plasma mixture the delay is much longer. It must be admitted that the plasma must first undergo a certain modification—to show itself ready to react with cytozyme—and this is expressed by saying that, in plasma, serozyme is found in the proserozyme state.

Calcified phosphate plasma being an excellent indicator of thrombin lends itself particularly to such experiments. The first phase of coagulation is shown by a modification such that the power to react promptly with cytozyme, i.e. the serozyme function, appears. Circulating blood includes pro-serozyme. It is not likely to react with cytozyme. This explains why (as Bordet, Delange, and Gratia have shown) even heavy intravenous injections of cytozyme are not dangerous, though in some degree they increase the coagulation of extracted blood. Fibrinogen being a passive element in coagulation does not participate in the production of thrombin. The first act of coagulation consists in the production of serozyme which unites with cytozyme and yields thrombin. This production is favoured by contact with glass or even by the influence of cytozyme itself.

Gratia has shown that by growing staphylococci in oxalated plasma they cause the coagulation of fibrinogen without the interference of the generator of thrombin and without altering these principles. Thus is obtained a defibrinogenized plasma, but which after all is still plasma. Rettger has shown (1909) that the amount of fibrin formed under the influence of thrombin is in strict proportion to the quantity of this principle. Nolf has strongly objected to Schmidt's enzyme theory. According to all probability thrombin is equally capable of uniting with antithrombin. The outcome of Nolf's experiments is that if under certain influences thrombin is produced in peptonized plasma, the latter loses its antithrombic power. Added to complete blood it no longer retards coagulation. According to Haycraft, Pekelharing, and Morawitz, hirudin neutralizes thrombin and also retards its production. The most important problem is to find out the order of the different phenomena whose 'ensemble' constitute the sum total of coagulation. It is also necessary to determine at what moment and in what manner each of the factors intervenes. There is also no reason why the same factors should not act in different ways at different times. Tissue juice owes part of its coagulating power to lipoidal cytozyme, but it also intervenes owing to a more alterable constituent (particularly sensitive to heat) whose mode of action is unknown. The most reasonable explanation is that this principle is endowed with pronounced adhesive tendencies which allow it to act as connecting link between the different elements which form coagulation. Thrombin produced in a liquid containing fresh tissue juice disappears quickly, doubtless by absorption. On the other hand, tissue juice reacts with blood-cells. It energetically agglutinates platelets, even in a calcified medium (Aynaud). Heating or treatment by mineral precipitants rids it of this power. Very probably it is to this coagulating principle accelerated by acetic acid (Wooldridge) that tissue juice owes its toxicity, which is greatly decreased by heating to 65° or by contact with kaolin (Czubalski, 1914). Hirudin, which retards coagulation, protects animals against the effects of an injection of the extract (Gley, Dold, and Ogata).

**Favourable influences and antagonistic factors.** If it is necessary to elucidate how blood coagulates it is also necessary to understand why in normal circumstances it remains fluid. Circulating plasma contains soluble calcium salts, but one must admit that the vessel-wall does not produce the identical effects of contact as with glass. This is the principal reason why the blood remains liquid in the vessels. We know that this principle, cytozyme, is normally situated, at least for the greater part, in the platelets. Here is definite proof that they would not in themselves suffice to protect the blood against all eventualities. A certain amount of diffusion of cellular principles in the liquid medium is *a priori* inevitable. Consequently, in order that the blood may remain definitely fluid *in vivo*, it must in itself possess a certain antagonistic factor of coagulation capable of ensuring equilibrium. From this a plasma endowed with normal composition will not coagulate *in vitro*; it must not, therefore, be inferred that it contains no trace of any principle necessary for coagulation. On this point Nolf has justly insisted. One can certainly say that it does not contain this principle in sufficient quantity. Birds' plasma coagulates when lipoidal extract of cells is put into it. As Nolf has shown, birds' plasma often coagulates when it is diluted with distilled water. We do not, however, ignore the fact that a strong saline concentration is opposed to the reactions which lead to the appearance of thrombin. It is easily shown that the best concentration for this process is lower than that of normal blood. Hence, birds' plasma, which contains proserozyme, is not completely free from cytozyme. It contains so little that the phenomena are only apparent under favourable conditions. It appears that in peptonized plasma antithrombin not only antagonizes the action of thrombin, but, above all, prevents its production. This antagonistic influence can be counterbalanced by the increase in quantity of one of the generators, the cytozyme, or by the intervention of thromboplastic influences such as the addition of distilled water or the increase of its means of contact with foreign bodies, &c.

**Examination of theories relating to the origin of thrombin.** According to Wooldridge, thrombin is not the primary and necessary cause of coagulation, but is the product of the latter. This idea has been taken up and developed by Nolf. Coagulation, according to this author, is the result of the union of three colloids, fibrinogen, thrombogen, thrombozyme. The two latter respectively arise from plasma and the blood-cells. They correspond to the thrombogen and thrombokinase of Morawitz. These substances have been considered to be of an albuminoid nature; the three colloids, being capable of uniting in variable proportions, can form complexes of different composition. That rich in fibrinogen is fibrin. The production of fibrin is the same condition as the appearance of thrombin. Fibrinogen thus necessarily intervenes in the production of this active principle. This theory is not in accordance with the above-mentioned investigations. The idea supported by Bordet and Delange, that the lipoid known as cytozyme showing the characters of lecithin is really one of the generators of thrombin, is not accepted by Nolf. The generator of thrombin which is thrown into the blood-stream by leucocytes or platelets, and which Nolf calls thrombozyme, has not, according to this author (and contrary to the opinion of Bordet and Delange), anything in common with the lipoid. Platelets heated to 100° C. accelerate coagulation as well as fresh platelets; the emulsion of lipoid extract behaves exactly the same as these. It is thus useless to suppose the existence of an active principle other than lipoid, and which would be Nolf's thrombozyme. While giving to the lipoids, particularly to one of them, namely, cephalin, a great importance in coagulation, Howell does not agree with the idea that substances of this type are really the formers of thrombin. He shows that the addition of lipoid to peptonized plasma brings about coagulation, but he admits that this substance acts by neutralizing antithrombin. He considers that the mother-substance of thrombin is unique, and only needs for its production the presence of calcium salts. No one denies the reality of antithrombin or the existence in perfectly normal blood of one or of several substances antagonistic to coagulation. But the question is whether cytozyme, when it provokes or accelerates coagulation despite the antithrombin, acts by directly neutralizing the latter, as Howell considers, or favours the appearance of an abundant thrombin capable of overcoming or even destroying the inhibitory influence of antithrombin. Howell's theory, in fact, does not appear to be in conformity with the experiments of certain investigators as related in the preceding pages.

Gratia has shown that cytozyme does not quantitatively neutralize hirudin. A little cytozyme provokes the rapid coagulation of a plasma to which a moderate addition of hirudin has been added, thus making spontaneous coagulation impossible. But any quantity whatsoever of cytozyme is powerless if the amount of hirudin in action surpasses a certain limit which is quickly attained. This is easily understood if it is admitted that it is thrombin and not cytozyme which produces antithrombin. On the other hand, the apparent neutralization of antithrombin by cytozyme takes place the more readily as the liquid is rich in serozyme.

Upon the whole the investigations of Gratia with reference to antithrombin do not agree with Howell's theory. On the contrary, they harmonize perfectly with the opinion of Bordet and Delange, according to whom cytozyme unites with serozyme to produce thrombin.

W. A. M. S.

**Vines, H. W. C. The coagulation of the blood. Part I. The rôle of calcium.** *J. Physiol.*, 1921, **55**, 86.

In all theories of coagulation the presence of calcium salts has been recognized as an essential factor, and it is generally held that the activity of the calcium depends on its presence in ionized form, though the method of its action is at present not clearly defined. This paper is an investigation of the state in which calcium is present in shed blood. It is found to be present in normal blood in two forms, ionized and combined. The latter is transformed into the ionic state during coagulation.

The addition to normal blood of oxalate, citrate, or fluoride in amount chemically equivalent to the total calcium of the blood does not inhibit coagulation. This indicates that the presence of ionized calcium is not essential to the clotting process. The anticoagulants described all inhibit clotting primarily by combining with the calcium-containing complex. The amount of anticoagulant required to neutralize the action of the complex is in each case in excess of the chemical equivalent of the calcium attached to it. Calcium combined with an organic substance at present not defined is the essential factor in the start of blood coagulation. This complex probably corresponds to the thrombokinase of Morawitz. W. A. M. S.

**Kohda, K. On the cultivation of *Bacillus leprae*.** *Kitasato Arch. Exp. Med.*, 1921, **4**, 141.

In 1910 Kedrowski, of Moscow, published an account of a bacillus which he believed to be *B. leprae.* The present author obtained a culture of this organism and has made it the subject of an investigation. He finds that it is acid- and alcohol-fast and develops on media similar to those which favour the development of the avian tubercle bacillus. When injected into guinea-pigs, rabbits, rats, and mice it showed trivial pathogenic properties and it manifested agglutinative and complement fixing interactions with the sera of lepers, but not in a degree that could be considered as specific. W. B.

**McJunkin, F. A. Tuberculin hypersensitiveness in non-tuberculous guinea-pigs induced by injections of bacillus-free filtrates.** *J. Exper. M.*, 1921, **33**, 751.

This is a study of the mechanism and nature of tuberculin hypersensitivity. When a guinea-pig with well-developed peritoneal tuberculosis is inoculated intraperitoneally with about 20 c.cm. of a heavy suspension of virulent tubercle bacilli death occurs as a rule within 24 hours or the animal shows marked symptoms of toxaemia. If the viscid fluid of a case of peritoneal tuberculosis is mixed with salt solution and passed through a Berkefeld filter a bacillus-free filtrate is obtained which induces in normal guinea-pigs a certain degree of cutaneous hypersensitivity to tuberculin. The abdominal organs and parietal peritoneum, to which masses of leucocytes and tubercle bacilli are adherent when crushed, extracted with saline yield filtrates which likewise bring about cutaneous hypersensitivity to tuberculin.

The hypersensitivity does not appear before the seventh or eighth day, and is therefore considered by the author to be the result of an active sensitization of the animal. W. B.

**Frouin, A.** Sur la teneur en matières grasses des bacilles tuberculeux des types humain, bovin, aviaire. [**On the fat content of bacilli of human, bovine, and avian types respectively.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 606.

The fat content of tubercle bacilli has been shown to vary between 8 and 46 per cent., and this has been attributed to the different solvents employed. The present author is of opinion that the chief factor is the type of the bacillus employed, for he finds that the *typus bovinus* in general yields a much higher percentage than the *typus humanus*, on all media, even those containing glucose instead of glycerine. The fat content of bacilli of avian origin approximated that of the bovine type. W. B.

**Renaux, E.** Sur l'homogénéisation des crachats tuberculeux et la recherche du bacille de Koch dans le pus d'abcès froid et d'adénites suppurées et dans les urines. [**On the homogenization of tuberculous sputa and the search for T. B. in cold abscesses, suppurative glands, and urines.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 833.

The method of the author consists of exposing the tuberculous exudate to a temperature of 120° C. in the autoclave for two or three minutes. After being cooled it is centrifugalized and to the deposit is added ten to twenty times its volume of soda (5 per 1,000). Solution of the deposit in the alkali is carried out in the water-bath, the fluid being then centrifugalized for 15 minutes. The slight deposit which remains is treated by the Ziehl-Neelsen method in the ordinary way, the counter-stain with methylene blue being omitted. The method can be carried out in about one hour, and, from the fact that the bacilli are dead, offers no risk of infection.

W. B.

**Liebhardt, E.** Der Nachweis aktiver Tuberkulose durch die Eigenharnreaktion von Wildbolz. [**Demonstration of active tuberculosis by Wildbolz's auto-urine reaction.**] *Ztschr. f. Tuberk.*, 1921, **34**, 99–102.

**Offenbacher, R.** Über die Untersuchung auf Aktivität der Lungentuberkulose nach Wildbolz. [**Investigations into the activity of pulmonary tuberculosis by Wildbolz's method.**] *Ztschr. f. Tuberk.*, 1920, **32**, 335–60.

**Trenkel, H.** Über die Brauchbarkeit der Wildbolzschen Eigenharnreaktion zur Feststellung der aktiven Tuberkulose. [**The value of Wildbolz's auto-urine reaction in the demonstration of active tuberculosis.**] *Beitr. z Klin. d. Tuberk.*, 1921, **47**, 219–30.

**Alexander, H.** Die Wildbolzsche Eigenharnreaktion als diagnostisches Hilfsmittel für aktive Tuberkulose. [**Wildbolz's auto-urine reaction in the diagnosis of active tuberculosis.**] *Ztschr. f. Tuberk.*, 1921, **33**, 321–32.

Liebhardt has tested Wildbolz's auto-urine reaction at the Communal Hospital in Nürnberg in 51 cases of pulmonary tuberculosis and other definitely non-tuberculous diseases. He experienced considerable difficulty in distinguishing between a positive and a negative reaction, and the decision in some cases depended on the sense of touch alone, a swelling, of the size of a pin's head, being otherwise hardly recognizable. He concludes that Wildbolz's reaction is definitely specific, depending on the presence of active tuberculosis; but it is insufficiently well-defined and constant to be of practical value.

Offenbacher has tested the reaction in Professor Strauss's hospital in Berlin in 20 cases of pulmonary tuberculosis, 19 of which were sputum-positive. Though he followed Wildbolz's directions in every detail, he obtained a definitely positive reaction only in three cases, and he believes that, while a positive reaction may be indicative of active tuberculosis, a negative reaction is of little importance.

Trenkel, of Dr. Amrein's Sanatorium at Arosa, also prefaces his unfavourable report on the reaction with the statement that he followed Wildbolz's technique in every detail. His material consisted of 11 cases of severe pulmonary tuberculosis, 13 cases of inactive, 'closed' tuberculosis, 3 cases of doubtful tuberculosis, and 8 cases without any evidence of tuberculosis. He obtained doubtful or negative reactions in active tuberculosis, and positive reactions in healthy persons, and he suggests that the reaction is simply a 'salt reaction'.

Alexander, of the Seehof Sanatorium in Davos-Dorf, has investigated Wildbolz's reaction 159 times in 91 cases, 76 of which were cases of pulmonary or bronchial tuberculosis. In 13 cases there was no definite clinical evidence of tuberculosis, and in 12 of these 13 the reaction was negative. It was, however, also negative in 15 of the cases of clinically active tuberculosis. In the cases in which the reaction was at first negative and later positive, a remarkable improvement in the patient's health was observed in the interval. In 39 cases control tests were made, the urine of one patient, whose auto-urine reaction was known, being injected into the skin of another, whose auto-urine reaction was also known. The majority of these control tests pointed to the reaction being specific. The conclusion drawn is that, in its present stage, the test is of little value when negative, but when positive it is fairly reliable evidence of active tuberculosis. Three other points may be noted. No relation could be established between the auto-urine and the intracutaneous tuberculin test; the former never gave a positive reaction with urine that had not been concentrated by evaporation, and the reaction was considerably weaker when evaporation had been carried out in an open water bath than when the concentration of the urine had been effected by evaporation in vacuo. C. L.

**Olitsky, P. K.,** and **Gates, F. L. Experimental studies on the naso-pharyngeal secretions from influenza patients. IV. Anaerobic cultivation.** *J. Exper. M.*, 1921, **33**, 713.

The previous work of the authors has been abstracted in *Medical Science* (1921, **4**, 266). In the present, their fourth, article they describe their attempts to cultivate anaerobically the substance which they believe to be a living although non-bacterial agent occurring in the form of 'bodies'. In anaerobic cultures these bodies, which could be stained by well-ripened Loeffler's blue, occurred at the bottom of the tubes and were two or three times longer in one direction than in the other—a form which the authors describe as 'bacilloid'. Their long axis measured 0·15 to 0·3 microns. Even in remote generations these bodies traversed Berkefeld V and N candles and were actually obtained from the filtered nasopharyngeal washings of patients in the first 36 hours of uncomplicated epidemic influenza. The bacilloid bodies are called *Bacterium pneumosintes* (σίντης, injurer or devastator) on account of the fact that when injected intratracheally in rabbits and guinea-pigs they induce effects on the blood and lungs which are not to be distinguished from those obtained with the nasopharyngeal secretions of patients in the early hours of epidemic influenza. From the pulmonic lesions thus induced the same organism was recovered in pure culture and on injection caused similar lesions in subsequent animal passage. Its pathogenic effect is not lost by prolonged artificial cultivation. The authors consider that we are at the threshold of knowledge of a group or class of minute micro-organisms which the anaerobic Smith-Noguchi technique has thrown open to exploitation. W. B.

**ANDERSON, RUTH A.**, and **SCHULTZ, O. T.** **Immunologic study of strains of *Bacillus pfeifferi* isolated from a case of meningitis.** *J. Exper. M.*, 1921, **33**, 653.

The authors deal briefly with the literature of cases of meningitis in which *B. influenzae* has been recovered, and they describe five-strains which they themselves have isolated from a case of meningitis in a child 17 months old. The strains came from spinal fluid, blood, nose, throat, and nasopharynx. Agglutination, fixation, and opsonic reactions of the five strains were compared and were found to have no definite relations the one strain with the other, although the strains from the nose, throat, and nasopharynx showed some slight analogy. The authors consider in general that the strain variations which have been shown to exist by immunological methods do not support the view that *B. influenzae* is related aetiologically to epidemic influenza unless it can be shown that such variations are due to the instability of the organism. W. B.

**MEYER, A. H.** Meddelelse om Kighosteundersögelser paa Statens Seruminstitut. [**Report on whooping-cough investigations at the State Serum Institute.**] *Ugesk. f. Læger*, 1921, **83**, 523.

Between February 1916 and September 1920, the Serum Institute in Copenhagen received 1,665 'coughing bowls' for examination. These bowls were of aluminium, and contained Bordet's culture medium; they were sent out by the Serum Institute to practitioners wishing to investigate possible cases of whooping-cough. Meyer tabulates his material thus:

| Stage of Cough. | No. of Cases. | W. C. Bacilli found. |
|---|---|---|
| Catarrhal stage | 134 | 100 = 70 % |
| First week of convulsive stage | 277 | 158 = 57 % |
| Second ,, ,, ,, ,, | 201 | 122 = 61 % |
| Third ,, ,, ,, ,, | 121 | 55 = 45 % |
| Fourth ,, ,, ,, ,, | 74 | 30 = 40·5 % |
| Fifth ,, ,, ,, ,, | 107 | 10 = 9 % |
| Stage unknown | 56 | |
| Whooping-cough doubtful | 45 | |
| Data missing | 41 | |
| Not whooping-cough | 559 | |
| Useless material | 50 | |
| | 1665 | |

In 914 of the 970 cases of whooping-cough, the stage of the disease was recorded. Of 134 patients in the catarrhal stage, 70 per cent. showed W. C. bacilli, whereas, of the 107 patients who had coughed for more than five weeks, only 9 per cent. showed W. C. bacilli. Thus, the bacteriological evidence tallied with the clinical experience that the infectiousness of whooping-cough is progressively less in the successive stages of the disease; when the convulsive stage has lasted five weeks, the patient may be regarded as practically non-infectious, although a few may remain as carriers. The recommendation is, however, made that children should be kept away from school for five weeks after the onset of the attacks, and not only for the four weeks laid down in 1916 as the isolation period. In another table Meyer shows how, with increasing technical skill, his staff has succeeded in demonstrating an increasing number of W. C. bacilli in the material sent to the Institute. He urges practitioners also to send specimens of blood for the complement fixation test, as this is often useful in deciding whether a cough which has lasted a long time is due to whooping-cough or not.

C. L.

**Thjötta, Th. Studies on bacterial nutrition. I. Growth of *Bacillus influenzae* in haemoglobin-free media.** *J. Exper. M.*, 1921, **33**, 763.

The author's work took its origin in a study of the cultivation of different microbes in broth containing mucus produced by mucoid bacilli such as Friedländer's bacillus, ozaena bacillus, and similar micro-organisms. A culture of Friedländer's bacillus was grown on plain agar. After 24 hours the growth was suspended in a few drops of plain broth and of the suspension thus obtained 0·5 c.cm. was added to 5 c.cm. of plain broth and was then heated for one hour at 60° C., sterility being determined. On such a medium *B. influenzae* was found to live and multiply up to 10 days at 37° C. Further experiments indicated that the growth-inducing substance exists apart from the bacteria producing it. Experiments were then made with cultures of *B. proteus*. After development had taken place the proteus cultures were killed by heat and centrifuged, the supernatant fluid being employed to test its power of supporting the life of *B. influenzae*. On such a medium influenza bacilli grew typically. It was also found that the growth-inducing emulsions and extracts can be boiled and filtered through Berkefeld candles without destroying their enriching properties. The author considers that the growth-inducing effect of bacterial extracts is possibly due to substances belonging to the class of the so-called vitamines.

W. B.

**Skajaa, K.** Om Influenza og Influenzapneumoni. En pathologisk-anatomisk og bakteriologisk Undersökelse. [**A pathological, anatomical, and bacteriological study of influenza and influenzal pneumonia.**] *Monograph published by Gade's Pathological Institute in Bergen*, 1921 pp. 225.

The epidemiological section of this study contains an analysis of reports sent to the Institute by practitioners in answer to a list of questions. The answers to two of the questions were strikingly unanimous. Not one practitioner had noticed any abnormal frequency of pneumonia after the influenza itself had died out, and, with only two exceptions, every practitioner had observed epidemics of pneumonia with several members of the same household affected. The pathological and bacteriological section of this study deals with 184 necropsies. In several cases of pneumonia the duration of the disease did not invariably determine the number of the bacteria found. Indeed, some of the most acute cases, with haemorrhagic oedema, were most highly infected, while few or no bacteria were found in cases of a fortnight's standing. Pfeiffer's bacillus is regarded as of even less importance than streptococci and pneumococci in the genesis of influenzal pneumonia, and the chief thesis of this section is that the unknown virus of influenza is the first and chief cause of influenzal pneumonia; secondary infection may impose certain late features on the manifestations of influenzal pneumonia, but that is all it does. Pfeiffer's bacillus was not once found during the first two waves of the epidemic, and its appearance during the later waves was quite sporadic. It settled on the subjects of influenza and healthy persons with strict impartiality, and during one and the same wave it did not appear as a well-defined strain; serologically, it exhibited a remarkable degree of diversity. It was never found in empyemata, the blood, or in other organs than the lungs and the respiratory passages. The condition of the lungs regarded as characteristic of the (unknown) virus of influenza is one of serous or haemorrhagic effusion into the parenchyma, resulting in diffuse consolidation and hepatization of the most dependent parts. This condition is comparable with that of 'gas-pneumonia'; the pulmonary veins are distended by clotted blood, and on section the lung is almost black, glistening, and smooth. These were the conditions found when the bacteriological examination was negative or showed only few microbes. It is argued that the epidemic occurrence of pneumonia depends not on the prevalence of special 'secondary' microbes in certain areas, but on massive infection by the unknown virus of influenza brought about by overcrowding and insanitary housing. The greater virulence of the second wave, as compared with that of the first wave of the epidemic is taken to indicate changes in the virus of influenza itself, rather than in changes in the 'secondary', facultative-pathogenic microbes. Throughout this work there are references to blind-alley researches into the causation of influenza.

C. L.

**DAVIDE, H. L.** Til influensans etiologi. **[The aetiology of influenza.]** *Hygeia*, 1921, **83**, 150, 177.

Davide's researches were made at the State Bacteriological Laboratory in Sweden, and dealt with two periods, the epidemic of the autumn of 1918, and that of the spring of 1920. In the first period 76 cases were examined bacteriologically; in the sputum of 37 cases of pneumonia, streptococci (*S. viridans* in 2 cases) were found in 27, pneumococci in 10. In the sputum of the 10 cases of uncomplicated influenza, streptococci, but no other microbes, were always found. Streptococci were also present in all the 14 cases of empyema; of the 15 cases examined *post mortem*, 12 showed streptococci, 3 staphylococci. Pfeiffer's bacillus was never found. Yet in this first series the bacteriological examination was made early in the disease. On the other hand, streptococci were almost invariably present, and in one case complicated by pneumonia and cholera-like diarrhoea, streptococci were abundant not only in the sputum and the lungs, but also in the faeces.

In the epidemic of 1920 the same methods of examination were adopted, and Pfeiffer's bacillus was now found in 12 out of 60 cases. It was instructive that the frequency with which this bacillus was found was comparatively great in a small, well-defined epidemic of uncomplicated influenza, affecting 25 persons at a naval station. In this epidemic, too, streptococci were very common, being found in the sputum of 16 out of 18 cases of pneumonia and in the sputum of 30 out of 32 uncomplicated cases of influenza. After discussing his agglutination and complement fixation tests in relation to Pfeiffer's bacillus, and admitting that they were not very illuminating, Davide points out that no reliable evidence has yet been produced in favour of Pfeiffer's correlation of his bacillus with the causation of influenza. On the other hand, there is much bacteriological, serological, and epidemiological evidence against such a correlation. But Pfeiffer's bacillus cannot be excluded from the list of microbes which give a sinister turn to the course of influenza. C. L.

**Jordan, E. O.**, and **Sharp, W. B.** **Influenza studies. IV. Effect of vaccination against influenza and some other respiratory infections.** *J. Infect. Dis.*, 1921, **28**, 357.

This paper is one of a series of investigations on influenza, another of which by the same authors has been abstracted in *Medical Science* (1920, **2**, 482). The work here detailed was carried out in connexion with the Influenza Commission established by the Metropolitan Life Insurance Company of New York. Other papers of this series have been abstracted in *Medical Science* (1921, **4**, 267).

A series of approximately 6,000 persons were under observation for a period of 7 months. About one-half were inoculated. Selection was by alphabetical alternation and the cases were obtained from three large schools and two hospitals for mental diseases. The vaccine used was made up as follows:

| | |
|---|---|
| Pfeiffer's bacillus | 500 million |
| *Streptococcus haemolyticus* | 500 ,, |
| ,, *viridans* | 500 ,, |
| *Pneumococcus* type I | 1000 ,, |
| ,, ,, II | 1000 ,, |
| ,, ,, III | 500 ,, |

The second and third doses contained twice these amounts.

A table is given showing the incidence of influenza and influenzal pneumonia in age groups in the inoculated and uninoculated. Influenza occurred in 4·1 per cent of the inoculated group and in 4·8 per cent. of the uninoculated. Seven cases of pneumonia with two deaths occurred among the 118 inoculated influenza cases, while twelve cases of pneumonia with two deaths occurred in the 152 influenza cases which had not received the vaccine.

Of 19 cases of pneumonia not associated with influenza, 6 had been inoculated and 13 had not been inoculated.

The authors conclude that it seems unlikely that any considerable degree of protection was afforded by the vaccine. G. T. W.

**Blanc, J.**, et **Pozerski, E.** La réaction de milieux biologiques une nouvelle méthode de notation et de mesure. [**Reaction of biological media; a new method of measure and notation.**] *Ann. de méd.*, 1920, **8**, 392.

This is an account of the measurement of the reaction of biological fluids. The paper is divided into four parts. There is first an explanation of the meaning of hydrogen-ion concentration, and the symbolic notation of Sörensen. Then the action of indicators is set forth, together with the details of the preparation of a graded series of standard colour solutions. The third part deals with the technique of the method. The indicators used are those described by Clark and Lubs. Lastly, the authors consider the results of the method, and also common applications to blood, serum, urine, and gastric juice. There does not appear to be much that is really new in the paper. W. A. M. S.

**Foster, L. F. The biochemistry of *Streptococcus haemolyticus*.** [**B.**] *J. Bact.*, 1921, **6**, 211.

Lactic acid appears to be the principal acid formed by *Streptococcus haemolyticus* in its fermentation of glucose broth. A smaller proportion of volatile acids is formed, made up chiefly of acetic, with perhaps a trace of formic acid. A quantitative study of the ammonia excretion of the streptococcus indicates that a 'protein sparing' action occurs in media containing available sugar to meet the energy requirements of the developing cells. The maximum periods of glucose utilization and acid formation in glucose and in glucose-serum broth are correlated with growth at a maximum rate, though a considerable lowering of $P^H$ occurs during the period when growth proceeds at a diminishing rate. The greatest increase in output of ammonia is correlated in a general way with the maximum periods of growth, glucose utilization, and acid formation. Associated with this increased output of ammonia is evident a corresponding decrease in amino-acids. This seems to be associated with the interval in which the organisms are making their growth. During this period, in which it is presumed the anabolic processes are actively under way, the organisms are utilizing amino-acids for structural purposes. This would cause the latter to decrease in concentration in the medium, and furthermore would produce an increased excretion of ammonia through the katabolism of a part of the absorbed amino-acids. Subsequent to the period in which the organisms have made their growth a rise in the curves of amino-acid formation is manifest. In the cultures containing horse serum this rise is initiated by the sixth hour; in the glucose culture it appears by the ninth hour. A decrease in ammonia output, in general, accompanies the rise in amino-acid formation. These findings indicate that a decreased utilization of nitrogenous materials ensues after the organism has passed its maximum period of growth, despite the fact that proteolysis continues. A marked difference in nitrogen metabolism between a passage strain and a laboratory strain of *Streptococcus haemolyticus* is noted during the first three hours of incubation in glucose serum broth. Whereas the passage strain shows a definite decrease in amino-acid output coupled with an increased ammonia excretion, the laboratory strain exhibits a decided increase in amino-acid output coincident with a slight decrease in ammonia formation. Whether or not this represents a permanent deviation in metabolism from continued transplantation upon artificial culture media is an undecided question. An extensive bibliography accompanies this communication. W. A. M. S.

**Foster, L. F. The relation of hydrogen-ion concentration to the growth, viability, and fermentative activity of *Streptococcus haemolyticus*.** *J. Bact.*, 1921, **6**, 161.

*Streptococcus haemolyticus* can ferment the common hexoses and disaccharides, but not the polysaccharides. The final hydrogen-ion concentration produced in broth containing different sugars varies between the limits $P_H$ 4·85 to 5·40. The lowest value is in broth containing glucose, and the highest in lactose broth. The characteristic final $P_H$ is seldom reached in the first generation but is usually attained by the second generation culture. Subsequent transplants do not show lower levels of $P_H$. Plain broth cultures of *S. haemolyticus* show a decrease in $P_H$ which is practically the same as that of cultures of the organism in sugar-free broth. This is believed to be due to a selective action upon that portion of the peptone molecule which Pick has shown reacts typically like a carbohydrate. *S. haemolyticus* can produce its characteristic final $P_H$ in neutral broth containing 0·2 per cent. glucose. Concentrations of glucose up to 1 per cent. have no further effect upon the level of the final $P_H$. The final hydrogen-ion concentration of the streptococcus is not influenced by the presence of $K_2HPO_4$ in concentrations up to 1 per cent., providing sufficient glucose is present. Titration curves show that horse serum in broth exerts a slight but distinct buffer effect. According to the author the curves of acid formation with time may be separated into five characteristic periods: stationary, lag, maximum, negative acceleration, and maximum stationary. Through an increase in the amount of inoculum or by employing a parent culture of suitable age as a source of inoculum it is possible to reduce the stationary and lag periods to a minimum. The presence of 5 per cent. horse serum in glucose broth reduces lag in acid formation by two to four hours. This may be due either to the presence of growth-accessory substances or to the presence of easily available nutritive materials. In glucose broth the maximum period of acid formation is initiated usually between the sixth and eighth hours, and is maintained for two hours. Maximum production of haemotoxin occurs between the sixth and eighth hours also. The most rapid formation of acid takes place in broth adjusted to a $P_H$ of 8·1 while the minimum is at 7·6. The optimum for acid formation is believed to lie at about 7·8. The limits of hydrogen-ion concentration which support the growth of *S. haemolyticus* are: minimum, plain broth 6·35, 1 per cent. glucose broth 6·35, 1 per cent. glucose and 5 per cent. serum broth 5·70. The corresponding maxima are 8·50, 8·50, 9·25. Acidity is the chief factor contributing to inhibition and death of the streptococcus in glucose broth cultures. This is evidenced by the fact that growth proceeds luxuriantly in filtrates from active cultures the acidity of which has been neutralized by a base. At a $P_H$ of 5·25 both lactic and acetic acids appear to have equal disinfecting powers for *S. haemolyticus*. Organisms live for longer periods in filtrates from active cultures than in broth brought to the same $P_H$ with lactic or acetic acids. A marked increase in tolerance for acid is shown by streptococci in the presence of horse serum. In one test it was found that the viability persisted for a period nearly four times as long in serum glucose broth of $P_H$ 5·20 as was evident in glucose broth adjusted to the same $P_H$. W. A. M. S.

**Foster, L. F.**, and **Randall, S. B.** **A study of the variations in hydrogen-ion concentration of broth media.** *J. Bact.*, 1921, **6**, 143.

Broth (beef infusion or beef extract) adjusted to $P_H$ values ranging from 5·0 to 9·0 undergoes a change in hydrogen-ion concentration upon autoclaving. This is most marked in media adjusted in the alkaline range 7·8 to 9·0, less great in the acid range 5·0 to 6·2, and usually inappreciable in the neutral range 6·6 to 7·4. The maximum change is about 0·4 $P_H$ and in the majority of cases is not above 0·2 $P_H$. The change is usually an increased acidity. Decreases in acidity were observed in a few instances, but these are exceptional. In media of the same composition the reaction changes are not necessarily uniform in different experiments.

Autoclaved broth undergoes changes in hydrogen-ion concentration upon standing. The degree of change is not influenced by the environmental temperature within the limits 10° C. (ice-chest) and 37° C. (incubator). The reaction changes on standing (as in the case of autoclaving) are most noticeable in the alkaline range, less marked in the acid range, and least in the neutral range. Neutral media usually do not change on standing. The change on standing is almost always in the direction of an increase in acidity.

Broth adjusted to various $P_H$ levels from 5·0 to 9·0 and exposed in tubes plugged with cotton to an atmosphere of $CO_2$ for twenty-four hours shows marked alterations in reaction. The change is always an increase in acidity, the greatest change occurring in the alkaline range. Upon allowing broth adjusted to various $P_H$ levels to stand in a $CO_2$-free atmosphere, the same reaction changes were noticed as in duplicate lots of broth allowed to stand in the air of the laboratory. The increases in acidity shown by broth on standing did not seem to be due to an absorption of atmospheric $CO_2$. Reaction changes in media of $P_H$ 5·2 to 9·2 do not appear to stand in relation to changes in formol-titrating nitrogen. The possibility of an increase in acidity of broth through the opening up of —COHN—groups during hydrolysis of the protein constituents suggested by Robertson remains a plausible one. W. A. M. S.

**Shearer, C. On the amount of heat liberated by *Bacillus coli* when grown in the presence of free amino-acids.** *J. Physiol.*, 1921, **55**, 50.

When *B. coli* is supplied with abundant free amino-acids already prepared, the process of building these into the living protoplasm is an extremely economical one, in which little energy is wasted. While different batches of tryptic digest gave widely divergent results in this respect (probably due to the fact that their amino-acid content was also very different), as compared with the growth of the same organism on glucose peptone broth, the process is from three to eight times more effective, although in the fermentation of glucose this germ would seem to use surprisingly little (about 1 per cent.) of the total energy available in the carbohydrate molecule.

Tryptic broth that has been digested about a week produces considerably more heat with *B. coli* than the same broth digested for a long time (3–8 weeks). This difference would seem to be far too great to be accounted for by the extra hydrolysis the polypeptids had undergone in the 3–8 weeks' fluid. The pathological process of metabolism, either with tryptic digest or any other culture fluid, is always accompanied by a greater liberation of heat than is given by the same amount of growth on the same medium under normal healthy conditions, so that pathological is less economical than normal growth. W. A. M. S.

**de Kruif, P. H. Dissociation of microbic species. I. Coexistence of individuals of different degrees of virulence in cultures of the bacillus of rabbit septicemia.** *J. Exper. M.*, 1921, **33**, 773.

The author carried out experiments with one of the Pasteurellae probably identical with the bacillus of rabbit septicaemia of Theobald Smith and actually isolated from spontaneous infections occurring in normal rabbits. Two types of microbes were shown to exist in cultures. The one named 'D' grew diffusely in serum and plain broth and formed rather opaque fluorescing colonies on serum agar. It was highly virulent for rabbits, and maintained its characters through many passages in serum or plain broth. The other type, named 'G', was found to form flocculi in fluid media and to develop translucent bluish colonies with little fluorescence. Its virulence for the rabbit was trivial. These characteristics were persistent. The two types possessed identical fermentation reactions. Rabbits surviving inoculation with the slightly virulent type 'G' were found to withstand multiple fatal doses of 'D'. Agglutination experiments also rendered an antigenic identity probable; community of antigenic character was made certain by absorption tests. Type 'D' in contact with immune serum flocculated well at 55° C., but poorly or not at all at 37° C., whereas type 'G' was agglutinated equally well at both temperatures. After being carried through 25 passages in serum and in plain broth, type 'D' retained all its characteristics. W. B.

**Christiansen, M.** Luftflegmone efter subkutane injektioner. [**Gas phlegmon following subcutaneous injections.**] *Hosp.-Tid.*, 1921, **64**, 225–34.

After discussing the fairly numerous disasters due to gas phlegmon as a sequel to subcutaneous injections of drugs such as caffein, Christiansen, of the Veterinary and Agricultural Serum Laboratory in Denmark, gives an account of his tests as to the sterility of drugs sold for hypodermic medication. As two cases of gas phlegmon observed during the last epidemic of influenza were given subcutaneous injections of digisolvin, as well as of caffein, the makers of the former submitted samples of their drug to tests for Welch-Fraenkel's bacillus. The 6 sealed glass bulbs examined, each containing 1·1 c.cm. of digisolvin, proved to be perfectly sterile; this was the expected result, as their contents had been heated to 100 C. for 20 minutes. But several of the 27 bottles provided with cork stoppers, and containing each 15 c.cm. of digisolvin, which had not been sterilized by heat and which had been made up with alcohol and glycerine, proved to contain facultative aerobic, spore-forming bacteria possessing the characteristics of *B. subtilis.* No gas phlegmon or other pathogenic microbes were found. Of 5 bottles, with rubber stoppers, containing 15 c.cm. of digalen (Hoffmann, La Roche), 4 proved to be sterile, and one contained an aerobic, spore-forming, Gram-positive microbe not pathogenic to guinea-pigs. It differed in many respects from the microbe found in the digisolvin bottles. Christiansen concludes that though he found no pathogenic microbes, his tests prove the superiority of the single-dose, glass-sealed bulb over the cork-stoppered bottle holding several doses for subcutaneous medication.

In another series of investigations he examined, at different stages of manufacture, samples of digisolvin artificially contaminated with the Welch-Fraenkel bacillus. Sterility was, to his surprise, achieved at the first stage; this consisted of filtration through paper of the pulverized digitalis leaves which had been 14 days in a 90 per cent. solution of alcohol. Further tests showed that not the alcohol, but the filtration, had rendered the filtrate sterile. Although the serum culture of the Welch-Fraenkel bacillus used had been carefully dried and pulverized, the retention of the microbes by the filter paper was probably due to their being attached to small, dry particles of the culture medium. Another series of tests showed that by heating an alcoholic extract for two hours at a temperature of 70° C., a drug such as digisolvin can be rendered sterile. The culture medium used by Christiansen for testing the sterility of drugs consisted of fresh horse's brain, finely divided, to which an equal part by weight of water was added. C. L.

**Alexander, H. L. Precipitin response in the blood of rabbits following subarachnoid injections of horse serum.** *J. Exper. M.*, 1921, **33**, 471.

In the treatment of cases of cerebrospinal meningitis by antimeningococcic serum the author observed peculiar reactions when the serum was first given intrathecally and was subsequently given intravenously. When the injection was being made into the blood-stream, or immediately after, there was flushing, a feeling of warmth, restlessness, followed by pallor, dyspnoea, cyanosis, vomiting, and prostration. Such manifestations were seen only when the serum injections were given in the above-mentioned sequence. The author investigated the phenomena in the rabbit treated in a similar manner, his results being set forth in a series of tables and diagrams. Rabbits which received a single dose of horse serum in the subarachnoid space produced precipitins in the blood in greater abundance, of higher titre, and of greater durability than those in control animals which received a like injection intravenously. Repeated subarachnoid injections of normal horse serum induced precipitin formation in the blood early. No anaphylactic manifestations were witnessed in rabbits treated repeatedly with subarachnoid injections of serum when the precipitin content of the blood was high. Anaphylactins, as determined by passive transfer of anaphylaxis, were demonstrated in sera with a high precipitin content. W. B.

**Levaditi, C., Marie, A., et Isaïcu.** Recherches sur la spirochétose spontanée du lapin. [**Researches on the spontaneous spirochaetosis of the rabbit.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 51.

This communication deals with the behaviour of a spirochaete, similar to *Treponema pallidum*, which was found in the genital organs and nares of tame rabbits by Arzt and Kerl in 1914. The present authors have studied three strains from rabbits and find that the microbe locates itself especially in the skin and does not become generalized. The disease may be transmitted by scarification and also probably by sexual congress. Thus a male rabbit infected on the prepuce conveyed the disease by coitus to a normal female, the latter showing vaginal lesions on the fifty-second day after exposure. An experiment proved that the spirochaete is innocuous to man. W. B.

**Brown, W. H., and Pearce, Louise. Superinfection in experimental syphilis following the administration of subcurative doses of arsphenamine or neoarsphenamine.** *J. Exper. M.*, 1921, **33**, 553.

The authors have carried out a series of experiments on rabbits to determine the effect of subcurative doses of arsphenamine and of neoarsphenamine upon the resistance to reinoculation with syphilitic virus. All the animals were inoculated in the testicle with the same virus and the experimental tests were conducted when the first cycle of testicular reaction was nearing its height. The rabbits with the most severe lesions were those employed in the experiment of treatment and reinoculation. The results showed (1) that the treatment employed was insufficient to cure any of the therapeutic control animals ; (2) that the infected controls were highly refractory to a second inoculation ; (3) that the treated animals were highly susceptible to a second inoculation of virus and although not cured of their original infection reacted to the second inoculation with the formation of lesions indistinguishable from those of the first infection ; (4) that in certain cases the treatment administered had rendered infected animals more susceptible to infection than the normal controls. These experiments have an important bearing on the question of superinfection and reinfection in man. Until the modern salvarsan era instances of a so-called reinfection were very rare, but since salvarsan was employed many cases of reinfection have appeared in the literature, and where they have occurred it has been assumed that the primary infection had been cured by the drug.

W. B.

**Rist, E.**, et **Strohl, A.** Études expérimentales et critiques sur le pneumothorax. [**Experimental and critical studies on pneumothorax.**] *Ann. de méd.*, 1920, **8**, 253.

If, several days after the establishment of an artificial pneumothorax, not complicated by a purulent exudate, the gaseous contents of the pleural cavity are analysed, it is found that their composition is sensibly the same in all cases. The phenomena which are produced after the penetration of gas into the pleural cavity are completely explained by the gaseous exchanges which ensue. These consist in a diffusion across the pleural membrane at a speed proportional to a particular coefficient for each gas, and to the partial difference of pressure on each side of the membrane.

The mechanism may be considered as brought about :

(*a*) By the resorption of the gaseous collection which is due to the fact that the atmospheric pressure diminished by the amount of partial tension of gas in an organic medium is greater than the difference of pressure developed on account of pulmonary elasticity and is known as negative intrapleural pressure.

(*b*) By the maintenance of the negative intrapleural pressure, in spite of the permeability of the walls of the pleural cavity.

(*c*) By the invariable composition, after a certain time, of the gaseous mixture. This composition is shown when the quantity of gas coming from the pleura is, in a given time, the same fraction of the remaining quantity for each of the composing gases. Thus a constant 'régime' is set up which maintains the same composition.

By the application of this latter proposition to the limits shown by experience, the authors consider they have proved that this constant 'régime' is set up between the gases present in the pneumothorax and those of venous blood. From these facts the authors deduce that venous blood contains oxygen in greater proportion than they had hitherto admitted. The resorption curves established by these principles show that when insufflation is made with pure nitrogen or with atmospheric air, the resorption period is preceded by a relatively short phase, during which there is an increase of the total amount of gas. This explains the phenomena of over-compression which occurs a few hours after the insufflations and which the authors have shown in the case of the introduction of large quantities of gas under raised pressures. These resorption curves explain the considerable difference observed in the duration of the resorption according to the gases introduced and the relative importance of the two phases of variable and constant composition for each of them. They enable us to understand several peculiarities in the modifications undergone in the composition of the introduced gases—peculiarities which to certain experimentalists appeared abnormal and contradictory to a purely physical theory of these phenomena.

In this paper the subject of pneumothorax receives full mathematical treatment, the main results being illustrated in a series of curves. By those particularly interested the original paper should be consulted.

W. A. M. S.

**Olmer, D., et Berthier.** Sur la détermination du volume de la cavité pleurale au cours du pneumothorax. [**On the determination of the volume of the pleural cavity in the course of pneumothorax.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 210.

Only one solution of this problem has yet been attempted, viz. that by Bard. He expressed the volume as a function of the intrapleural pressure, before and after it had been put into communication with the pleura by a vessel of known volume containing a gas at a known pressure. Rist and Strohl showed that Bard's formula was incorrect. In order to study the variations in volume of a pneumothorax, the author investigates the diffusion of a given quantity of an easily diffusible gas, oxygen. The following is briefly the mathematical argument:

Let $X$ be the volume of the cavity, $X^1$ the volume of the gas in $X$ measured at atmospheric pressure and external temperature. $Q$ is the total quantity of oxygen contained in $X^1$ at the start. At the end of the first inspiration, let the volume $b$ of oxygen be absorbed from a volume $a$ of the gaseous intrapleural mixture. Let $l = b/a$. Now inject a volume of oxygen $V$ into the cavity. At the end of a second inspiration, determine the volume $b^1$ of oxygen contained in a volume $a^1$ of the new gaseous mixture, and let $L = b^1/a^1$.

$$\therefore l = b/a = Q/X^1 \text{ and } L = (V+Q)/(X^1+V.)$$

From this one easily finds that $X^1 = V(1-L)/(L-l.)$ Note that $X^1$, $V$, $a$, $b$, $a^1$, $b^1$, are all volumes at atmospheric pressure and the same temperature. To determine $X$, the real value of the capacity studied, one must take account of the pressure $p$ and the temperature of the intrapleural space. Let $H$ be the pressure of the atmosphere, then by Mariotte's (Boyle) law one may write $X = X^1H/p$. The author shows that this correction is negligible. The temperature of the intrapleural cavity is about 38° C. and the average external temperature 15°. Hence the application of the usual physical formula $V = V_0 (1 + at)$ leads to a correction of about 0·08 $X^1$. Details of the technique follow. A comparison of the results obtained on a dog by Bard's method and that of gaseous mixtures advocated by the author is given. It is concluded that Bard's method is inexact but simple, while that of the author is more exact, but a purely laboratory one, which cannot be used in general practice. W. A. M. S.

**Krumbhaar, E. B.**, and **Masser, J. H.**, jr. **Studies of the blood of normal monkeys.** *J. Med. Research*, 1921, **42**, 105.

The authors record their observations on blood counts of 13 normal monkeys (*Macacus rhesus*) varying in weight from 2,050 to 6,020 gm. The erythrocytic count showed an average of 5,985,000 per c.mm. with extremes of 7,140,000 and 5,060,000. The average number of leucocytes was 13,375, the lowest count being 8,900. The average differential count for 12 of the animals was as follows: polymorphonuclear neutrophiles 47·4 per cent.; lymphocytes 46·5 per cent.; large mononuclear and transitional forms 4·9 per cent.; eosinophiles 1·0 per cent.; basophiles 0·2 per cent. In comparison with man the polymorphonuclear cells showed a large number of lobes in nuclei, up to 15 being counted. The lymphocytes were usually larger than in man. Reticulated erythrocytes were rarely found and never in numbers higher than 0·3 per cent. of all reds. In six animals the platelet count was 267·166 on an average. A short analysis of the finding of other observers is given by the author for comparison. W. B.

**Bunting, C. H.**, and **Huston, J.** **Fate of the lymphocyte.** *J. Exper. M.*, 1921, **33**, 593.

The authors carried out a series of experiments on rabbits to determine the fate of the lymphocytes which reached the blood circulation by the large lymphatic trunks and especially the thoracic ducts. Direct counts taken from the duct immediately after death showed 20,000 to 50,000 cells per c.mm., 80 per cent. of them being lymphocytes. Splenectomy and other operative measures were employed to cut off the inflow of lymphocytes into the circulation and thus to determine the rapidity of their disappearance from the blood-stream. In one case there was a drop in the number of lymphocytes of 4,430 per c.mm. in six hours; on a basis of 100 c.c. of blood this would represent a disappearance of 443 million lymphocytes. A search of the organs led the authors to the belief that the great majority of the lymphocytes enter the mucous membrane of the gastro-intestinal tract and pass through it into the intestinal lumen, and it is in these sites that the function of the lymphocyte is normally performed. W. B.

**Ellermann, V.** **A new strain of transmissible leucemia in fowls (strain H).** *J. Exper. M.*, 1921, **33**, 539.

The author, who has already published, in Danish and German, a large number of important papers on transmissible leukaemia in fowls, deals here with a new strain isolated from a hen in 1917 and transmitted through 12 generations of fowls. In all, 122 birds were inoculated, positive results occurring in 34 instances (28 per cent.). The blood picture was characterized by myelocytes and large lymphoid forms, histological examination revealing interstitial deposits of myelocytes in the liver, spleen, and kidneys. An increase in virulence was observed during passage, as was shown in the shortening of the interval between the inoculation and the death of the animal. In the first animal of passage this period was $>133$ days, whereas in the twelfth it was 29 days. The increase in virulence did not affect the number of successful inoculations, which remained approximately constant in from 20 to 40 per cent. of the birds employed. As in the case with previous strains studied by the author, the new strain 'H' manifested itself in various forms both of myeloid and intravascular lymphoid types. A single lymphatic case was observed. In some instances of the intravascular type a diminution in the haemolytic power of the serum for the corpuscles of the rabbit was observed. Active immunization could not be produced by the subcutaneous inoculation of virulent material. As in previous work by Ellermann and Bang, it was found that the virus 'H' was a filter passer. Attempts to transmit human leukaemia to fowls were unsuccessful. In connexion with the above researches attention may be called to Ellermann's *Hönse-leucosen i Komparativ-patologisk belysning*, published in Copenhagen in 1920. This contains an admirable account of the author's extensive and important work on leukaemia in fowls. W. B.

## BIOCHEMISTRY

**Hopkins, F. G. On an auto-oxidizable constituent of the cell.** *Bio-Chem. J.*, 1921, **15**, 286.

One of the chief aims of biochemists of recent years has been to obtain some evidence of the nature of those substances which either are concerned in facilitating chemical action within the cell or produce changes which are important from a physiological or pathological point of view. Some substances such as ricin have been prepared in a state of great potency and presumably of a high degree of purity, but so far we have no knowledge of their constitution. Even at the present moment opinions are divided as to whether substances such as diphtheria toxin are of protein origin or are to be associated with the lipoids. In this important paper Hopkins has for the first time isolated from the cell a substance of definite chemical constitution which performs *in vitro* some of the catalytic phenomena which are closely connected with the fundamental activity of the cell. The substance isolated is one that performs the reduction of sulphur to hydrogen sulphide, which was observed by de Rey-Pailhade many years ago and to which he gave the name of philothion. By a very laborious process the substance may be isolated from yeast or from animal tissues (liver &c.), and proves to be a dipeptide composed of a molecule of glutamic acid and of cystein. The amount that is present is of the order of 0·01–0·02 per cent. of fresh tissue. It can be oxidized or reduced under the influence of factors known to be present in the cell, and therefore is in a condition to hand on hydrogen in the true manner of a catalyst. C. G. L. W.

**Plimmer, R. H. A.** 'Analyses and Energy Values of Foods.' *London, H.M. Stationery Office*, 1921, pp. 255.

For the composition of food materials those who are interested in problems connected with feeding have been obliged to use the tables compiled by König or the series of analyses furnished in Bulletin 48 of the U.S. Department of Agriculture. In some instances it has been possible to get special information from isolated articles, but all these data suffer from a lack of uniformity in the methods of analysis employed, and their utility to English workers is impaired in that they do not correspond to the conditions under which food is delivered in England at the present day. A considerable debt is owed to Dr. Plimmer for the set of 900 analyses embracing the composition of all the more important food products. The analytical methods are given and a short and useful commentary on the sampling accompanies the analyses. Appended are the tables from the Medical Research Committee's Report (1919) on the content of accessory food factors. The work was done for the Army Medical Service. C. G. L. W.

**Shorten, J. A., and Ray, C. B. The antiscorbutic and anti-beri-beri properties of certain sun-dried vegetables.** *Bio-Chem. J.*, 1921, **15**, 274.

Sun-dried tomatoes, potatoes, and cabbage retain to a considerable extent the antiscorbutic properties of the fresh vegetables. Sun-dried carrots, spinach, turnips, and turnip-tops have little or no antiscorbutic properties.

Sun drying does not affect the antiscorbutic quality of any of the vegetables examined. Cooking has a deleterious effect on the antiscorbutic property. The vegetables should be given in the form of salads.

C. G. L. W.

**Paton, D. N., and Watson, A. Aetiology of rickets.** *Brit. J. Exper. Pathol.*, 1921, **2**, 79. (*Physiol. Abstr.*, 1921, **6**, 201.)

In young dogs under laboratory conditions a liberal allowance of milk fat up to even 14 gm. per kilo body-weight does not prevent the onset of rickets. Pups kept largely in the open air may escape the development of rickets on an intake of less than 1·0 gm. of milk fat per kilo body-weight. With scrupulous care as to cleanliness it is, at least sometimes, possible to rear pups free of rickets in the laboratory on an intake of only 0·5 gm. of milk fat per kilo of body-weight, along with bread, provided that the diet contains an adequate supply of energy. The energy value of the diet, however supplied, quite apart from the presence of any hypothetical antirachitic factor in milk fat, would seem to play a part in controlling the development of rickets, but that it is only a contributory part is shown by the development of rickets in pups with a high energy intake if confined in the laboratory without such care. Milk fat may be reduced to 0·3 gm. per kilo of body-weight, if its place be taken by an equivalent amount of lard, without the onset of rickets. These observations give no support to the conclusion that rickets is a deficiency disease due to the lack of an antirachitic factor in the diet. C. G. L. W.

**Osborne, T. B., and Mendel, L. B. Ophthalmia and diet.** *J. Am. M. Ass.*, 1921, **76**, 905. (*Physiol. Abstr.*, 1921, **6**, 201.)

In experiments on unselected rats xerophthalmia was only seen in animals with deficient fat-soluble vitamine; in this group the incidence was 50 per cent., most of the cases developing before any marked decline in body-weight occurred. Administration of vitamine A (e. g. 0·1 gm. of butter fat per day) caused disappearance of the eye disorder, even though in some cases the animal subsequently died. C. G. L. W.

**Woodman, H. E. A comparative investigation of the corresponding proteins of cow and ox serum, cow's colostrum and cow's milk by the method of protein racemization.** *Bio-Chem. J.*, 1921, **15**, 187.

Immunity reactions and the chemical tests of the proteins of the blood and of the milk have given different results, the former showing that the two are identical, while the chemical tests have demonstrated a certain difference. By a method of racemization of most carefully purified proteins from serum and from colostrum by means of sodium hydroxide it has been shown that the globulins of cow and ox serum are identical with those of cow's colostrum. Lactalbumin and serum albumin are two distinct substances, hence a distinct mammary synthesis is necessary for lactalbumin as for caseinogen. C. G. L. W.

**Bogendörfer, L.** Über das Verhalten des Blutes und Körpergewichtes nach Schweissverlusten und Theocingaben bei halogenreicher und halogenarmer Ernährung. [**The effect of sweating and diuretics on the blood and body-weight with diet rich and poor in salt.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **89**, 252.

Loss of weight through sweating, and the regaining of the weight by subsequent water-drinking is dependent on the condition of the body when the sweating and administration of water takes place. The principal factor is the salt content of the body.

Body-weight is regained by water-drinking in 24 hours on ordinary diet. When the diet is poor in common salt the weight is only regained when sodium chloride is administered with the water. Sodium bromide may be used to replace sodium chloride.

By using diuretics such as theocine, the loss of weight through elimination of water by the kidneys is much greater in subjects who have had a salt-poor diet. Hence in using diuretics it is important to keep the salt content of the diet at a low level.

After a Turkish bath and a salt-poor diet the number of erythrocytes rises. C. G. L. W.

**Oehme, C.** Die Regulation der renalen Wasserausscheidung im Rahmen des ganzen Wasserhaushaltes. [**The secretion of water by the kidney in relation to general water metabolism.**] *Arch. f. exper. Path. u. Pharmarkol.*, 1921, **89**, 301.

This investigation concerns itself with the factors which influence the excretion of water by the kidneys. The experiments were performed on rabbits, which to a certain extent limits their general application. It would appear, from the results obtained, that neither nervous influences, hormones, nor change in the demand for water by the body determine the excretion of water by the kidneys, although the first and third of these factors may play a subordinate rôle. The principal agent in determining diuresis after the administration of water is the previous metabolic history of the subject. The diuresis is the resultant of the state of the blood and of the kidneys. It is therefore necessary in all tests for disturbed renal function to put the individual into a standard state of metabolism before applying a test.

C. G. L. W.

**Gad Andresen, K. L.** Die Verteilung des Harnstoffes im Organismus. [**The distribution of urea in the organism.**] *Biochem. Ztschr.*, 1921, **116**, 268.

This forms a very long and complete study of the amount of urea in various parts of the body. The general conclusions can be summarized as follows: The partition coefficient between plasma and blood-corpuscles is 0·8 approx. The partition coefficient between the plasma and the organic secretions is 1·0. Between plasma and tissues it is 1·0, if the fat is excepted. Between water-free fat and plasma the partition coefficient is 0·07. The tears and perspiration are exceptions. R. A. P.

**Stepp, W.**, and **Feulgen, R.** Über die Identifizierung der aldehydartig reagierenden Substanz im Harn von Diabetikern als Acetaldehyd. [**The identification of the aldehyde-like substance in diabetic urine as acetaldehyde.**] *Ztschr. f. physiol. Chem.*, 1921, **114**, 301.

The blood and urine of diabetics have been found to contain acetaldehyde. It appears in the urine only during acidosis, most regularly at the beginning and during the rise of this condition, although sometimes it is not found at all. In many cases, however, it occurs in considerable quantity, sometimes forming as much as 30–50 per cent. of the fractions usually determined as ‘total acetone’. The authors have identified it chemically by means of its compound with dimethylhydroresorcin, a substance used by Neuberg under the name ‘Dimedon’ for isolating acetaldehyde in the process of alcoholic fermentation. H. W. D.

**Bornstein, A.** Ueber Adrenalinglykaemie. [**On adrenalin glycaemia.**] *Biochem. Ztschr.*, 1921, **114**, 157.

The effect of injecting adrenalin into the human subject is to cause an increase of lung ventilation and consequent temporary rise in the respiratory quotient due to elimination of $CO_2$. The R.Q. then sinks after a few minutes to the normal or below it, and there comes on a hyperglycaemia. This is not correlated with increased carbohydrate consumption.

The experiments were made on normal and diseased persons. The author divides glycaemias into two classes. In one of these, such as the glycaemia induced by feeding, there is an increased carbohydrate consumption. In the other, of which adrenalin glycaemia is an example, there is no evidence of increased carbohydrate utilization. R. A. P.

**Zondek, S. G.** Die Bedeutung kolloidaler Nährlösungen für die Funktion des normalen, erschöpften und vergifteten Herzens. [**The importance of colloidal nutrient solutions for the normal, exhausted, and poisoned heart.**] *Biochem. Ztschr.*, 1921, **116**, 248.

This is a critical paper dealing with the cause of the improving effect in transfusion experiments of adding gelatine, gum arabic, or other colloid to the transfusion fluid. As will be familiar to many, the theoretical grounding of Prof. Bayliss's suggestions lies in the fact that the presence of a colloid in the fluid gave an osmotic pressure more approximating to the condition found in the blood. Zondek has come to the conclusion, from experiments upon the frog's heart, that the beneficial effect of such solutions is due to the presence of a small amount of calcium in the ash of the colloid. With gums such as tragacanth, which he states contain no calcium or very little inorganic salt, he obtains no beneficial effect. He thinks, therefore, that the gum saline can be replaced by a solution of which the calcium content is raised.

This suggests an interesting point which will be doubtless cleared up by future work upon the mammal. R. A. P.

**Wright, A. E. 'Intertraction' between albuminous substances and saline solutions.** *Proc. Roy. Soc.*, 1921, **92 B**, 118. (*Physiol. Abstr.*, 1921, **6**, 221.)

It is well known that Wright's treatment of septic wounds, so much in evidence during the recent war, consists essentially of the application of hypertonic salt solutions. The idea underlying it is the existence of a tractor or drawing force ('intertraction'), which, co-operating with diffusion, draws the putrid discharge with its contained bacteria out of the wound. In the present paper this is supported by experiments, the essence of which is that if serum or similar albuminous fluid is placed on the surface of a strong salt solution, the serum, which is the lighter fluid, rapidly sinks into the heavier saline medium, and remains at the bottom. It is suggested that the serum enters into conjunction with salt, and so becomes heavier, and that the saline solution, parting with its salt, simultaneously becomes lighter; the proteins do not fall out of solution. C. G. L. W.

**Parnas, J. K.**, und **Laska-Mintz, E.** Beeinflussen subminimale Reize den Ablauf chemischer Umsetzungen im isolierten Muskel? [**The influence of subminimal stimuli upon the course of chemical changes in muscle.**] *Biochem. Ztschr.*, 1921, **116**, 59.

The research was directed to the question whether it was possible to produce chemical change in a muscle by the use of subminimal stimuli, which produced no mechanical change. This was a question propounded by Heidenhain and Gottlieb. Lactic acid determinations were made by the Parnas modification of the von Furth and Charnass method. The authors could find no evidence of the appearance of lactic acid in the muscles which had been treated with subminimal stimuli. They could also find no apparent difference in acidity. Frog's muscle was used in the experiments.
R. A. P.

**Parnas, J. K.** Über den Kohlenhydratstoffwechsel der isolierten Amphibienmuskeln. [**On the carbohydrate metabolism of isolated amphibian muscle.**] *Biochem. Ztschr.*, 1921, **116**, 71.

The trend of the recent work by Meyerhof, following upon the work of Parnas and Wagner, has been towards the elucidation of the relation between the lactic acid appearing in the muscular contraction, and the store of glycogen in the muscle. It was shown with great clarity by the work of Fletcher and Hopkins that lactic acid appeared readily in muscle in the absence of an efficient supply of oxygen. Later it has appeared from the work of Embden and others that the lactic acid arises from a precursor of a hexose-phosphate nature. The problem of the relation of this so-called lactacidogen to the glycogen of the muscle has been attacked lately with success by Meyerhof. He has found that there is a balance between the amount of lactic acid in a muscle and the glycogen store of the muscle. He has further obtained evidence that in the process of the recovery of a muscle some of the lactic acid appearing is reconstituted, only a small part being actually burnt.

The present paper by Parnas deals with the relation between the amount of glycogen used by a muscle and the work done by it. The efficiency of the sartorius comes out as about 50 per cent., when calculated in this way—a figure practically the same as the one obtained by A. V. Hill from considerations of the heat-production in contraction. It is considered that the correspondence between the two different methods of measurement are strongly in support of the view that carbohydrate really supplies the contractile substance. R. A. P.

**Abelin, J.** Ueber den Einfluss spezifisch gebauter Iodverbindungen auf die Metamorphose von Froschlarven und vom Axolotl. [**On the influence of specific iodine compounds upon the metamorphosis of frogs' larvae and of the axolotl.**] *Biochem. Ztschr.*, 1921, **116**, 138.

This is a continuation of former work, in which it was shown that diiodotyramin had more influence upon the development of frogs' larvae than tyramin.

Compounds consisting of iodine linked to protein breakdown products were proved to be of great importance in the initiation and the continuance of the metamorphosis of frogs' larvae. The compounds tried were diiodotyrosin and an iodized protein. A number of other compounds of iodine tried, such as diiodosalol were without effect. The effects obtained with the diiodotyrosin imitated the effect of thyroid extract. Diiodotyrosin was also able to bring about the metamorphosis of the axolotl.

It appears from this that iodine in a special combination is essential for this growth factor. If so, it would seem that there still remains to be explained the reason why it is an iodine tryptophane compound that has been isolated from the thyroid gland by Kendall. R. A. P.

**Wuth, O.** Ueber biologische Wirkungen proteinogener Amine. Zugleich ein Beitrag zur Frage der Acetonitrilreaktion. [**On the biological effect of proteinogenous amines. A contribution to the question of the acetonitrile reaction.**] *Biochem. Ztschr.*, 1921, **116**, 237.

The author has made use of a reaction found by Reid Hunt to investigate the parallelism between the effects of thyroid extract and of tyramin and diiodotyramin.

The reaction in question is as follows: Mice when treated previously with thyroid extract stand larger doses of acetonitrile ($CH_3CN$) than the normal. Using this acetonitrile reaction, it was found that tyramin and diiodotyramin, when given to mice for some time before treatment with acetonitrile, rendered the mice much more resistant to the latter. In this respect the results agreed with those of thyreoidin. Histamin on the other hand, was without effect R. A. P.

**Falta, W.,** und **Richter-Quittner, M.** Ueber die chemische Zusammensetzung der Blutkörperchen. [**On the chemical composition of the blood-corpuscles.**] *Biochem. Ztschr.*, 1921, **114**, 145.

This is a reply to the critics who have disbelieved in the results of the previous work by these authors upon the content of blood-corpuscles in sugar. The disbelievers quoted are Ege, Hagedorn and Gad Andresen, and Warburg. In extension of the original work, the authors hold that human blood-corpuscles under physiological conditions, besides containing no sugar, rest nitrogen, or chlorine, contain no calcium or cholesterin-ester. According to the work here, the following factors outside the body may cause the entry of sugar into the corpuscles: standing of the whole blood at any temperature, —defibrination by shaking with a glass or wooden rod,—too long or too powerful centrifuging,—freezing of the corpuscles,—addition of calcium precipitants, especially if the concentration of these is too large.

The authors' opinions are supported by experimental tables.

R. A. P.

**Fürth, Otto,** und **Lieben, F.** Colorimetrische Untersuchungen über das Tryptophan. IV. Ueber die Melanoidinbildung bei der Säurehydrolyse von Proteinen und ihre Abhängigkeit von Tryptophankomplexen. V. Zur Kenntnis der Immunsera und ihres Tryptophangehaltes. [**Colorimetric experiments on tryptophane. IV. On the formation of melanoidin in the acid hydrolysis of proteins and its dependence upon tryptophane complexes. V. On our knowledge of the proteins of immune sera and their tryptophane content.**] *Biochem. Ztschr.*, 1921, **116**, 224.

As the result of some work in which the colorimetric method of estimating tryptophane is employed, the conclusion is reached that the dark-coloured acid insoluble condensation products which appear during the acid hydrolysis of protein are degradation products of tryptophane. It is proposed that these products should be classed as melanoidin. The term melanin should be reserved for the natural pigments, and humin for the dark products which are the result of carbohydrate change.

In the second paper the results of an investigation of horse serum are given. Sera from horses immunized for diphtheria, dysentery, and tetanus were analysed as regards their protein and tryptophane content. It was found that there was an increase in the globulin fraction of the serum, especially the pseudoglobulin part. There was, however, no evidence of abnormal tryptophane content of the individual protein. R. A. P.

**Kossel, A.,** und **Giese, G.** Über den Chloromfarbstoff. [**On the colouring matter in chloroma.**] *Ztschr. f. physiol. Chem.*, 1921, **114**, 127.

The green colour of chloroma tumours is held to be due to a deposit of iron sulphide. The iron content of the tissue is fairly high. The conditions under which soluble sulphides are produced are not known, but it is pointed out that a similar green deposit of iron sulphide is formed at the boundary of the yolk of a hard-boiled egg. H. W. D.

**Schenk, P.** Über die Wirkungsweise der β-Imido-ozolyläthylamins (Histamin) auf den menschlichen Organismus. [**The action of histamin on man.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **89**, 332.

Subcutaneous injections of histamin produce vaso-dilatation in the head and in the splanchnic area, vomiting, and bronchial spasm. The stomach shows hypertonic total contraction. All these symptoms are practically completely suppressed by adrenalin. Paraoxyphenylethylamine exerts a like influence on histamin action. Th adrenalin glycosuria is not influenced by histamin. The action of the drug is due to paralysis of the sympathetic or the myoneural junction between nerve and muscle.

C. G. L. W.

**Hunt, Reid. Some factors relating to the toxic action of arsphenamin.** *J. Am. M. Ass.*, 1921, **76**, 854. (*Physiol. Abstr.*, 1921, **6**, 219.)

The symptoms in rats caused by m-amino p-hydroxyphenylarsenous acid ('arsenoxide') are very characteristic, and the presence of traces of the oxide in arsphenamine is readily detected by these. By treatment of the drug with sodium hydrosulphite the toxicity due to the presence of the oxide is at once diminished. The toxicity of commercial arsphenamine is not due to the presence of the oxide, since it is often greatly diminished by standing or warming; this toxicity is probably due to the physical state of the solution. In other cases toxicity seems to be due to the inorganic arsenic or unidentified impurities.

C. G. L. W.

**B. Schick.** Der Icterus neonatorum eine Folge des Abbaus mütterlichen Blutes. [**The breaking down of the maternal blood as the cause of icterus neonatorum.**] *Ztschr. f. Kinderheilk.*, 1921, **27**, 233. (*Physiol. Abstr.*, 1921, **6**, 215.)

The maternal blood is destroyed in the human placenta, and the red corpuscles and their haemoglobin absorbed by the cells of the chorionic ectoderm. It forms the source of iron for the foetus. This maternal haemoglobin is the mother-substance of the bilirubin, which causes jaundice. The final changes into bilirubin take place in the foetal liver. The chorionic epithelium acts like the spleen, and produces intermediate stages in bilirubin formation. Icterus neonatorum is regarded as a physiological occurrence.

C. G. L. W.

**Holker, J. Methods of measuring the opacity of liquids.** *Bio-Chem. J.*, 1921, **15**, 216.

An instrument is described in which a platinum wire is obscured by the opacity of the liquid examined. It can be used for determining quantitatively the opacity of liquids and can therefore be used for studying serum and other reactions in which a suspension of fine particles is produced.

C. G. L. W.

# RADIOLOGY AND ELECTROLOGY

## *Radio-diagnosis.*

**RAHNENFÜHRER, C.** Beitrag zur Klinik der umschriebenen Lungeneiterungen (Abszess und Gangrän). [**Communication on the clinical history of circumscribed pulmonary suppuration (abscess and gangrene).**] [**B.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen,* 1921, **28**, 97.

A somewhat voluminous description—with clinical records—of this variety of case. The author himself saw 30 cases in 2½ years at the Municipal Hospital of Magdeburg-Altstadt, and concludes that the condition is not so uncommon as is usually supposed. Frequently the lung condition is overshadowed by a secondary empyema and therefore escapes recognition, and in many instances it is mistaken for tuberculosis. He describes it as supervening on croupous pneumonia, influenzal pneumonia, tuberculosis, neoplasm, and trauma. In these instances it is dependent upon aspiration—whether the bronchi be normal originally or not; in other instances he ascribes it to embolism or to lymphatic absorption. Radiological examination was made in 19 cases; sometimes radioscopy was useful, but most information was given by radiography, particularly if stereoscopic. Usually a cavity was demonstrated by this means, but was associated with a dense shadow of irregular shape due to surrounding consolidation. Separate sections of the paper are given to symptomatology, complications, prognosis and statistics, diagnosis and differential diagnosis, and to therapy. A good bibliography and some clear radiographs are included, but in the main the paper is clinical. W. S. L.-B.

**GROEDEL, F. M.** Abgekapselte Pleuritiden im Röntgenbild. [**The radiological appearances of encapsuled pleural effusions.**] [**B.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen,* 1921, **28**, 137.

The paper is illustrated by three photographs and 19 line drawings in the text. The seats of predilection for such encapsuled effusions are indicated and especial stress is laid upon the importance of the posterior mediastinal space in this connexion. W. S. L.-B.

**JOSSE, M. H.** Radioscopie et radiographie pulmonaire. [**Pulmonary radioscopy and radiography.**] *Soc. de méd. mil. franç.*, 1920, Nov. 4. (*Arch. d'électric. méd.*, 1920, **28**, 365.)

From the examination of some thousands of cases the author concludes that even if the radioscopic examination maintains an unquestionable superiority for the study of the cardio-pleuro-pulmonary function, it is very often insufficient for the study of certain pulmonary conditions. Lesions with advanced granulation, the existence of small cavities in the region of the hilum, are often not recognized by a screen examination, are mistaken for shadows or the marbling of the lung tissues, when they are very clear on radiographic examination. Radiography cuts down the unavoidable diversities of estimation in radioscopy, diversities depending on the apparatus or the observer. It alone forms a perfect clinical or medico-legal record. Pulmonary radiographs should be taken at a distance from the anticathode to the plate of 1½ metres at least; the subject should be in the upright position, forced inspiration, the arms extended and placed so as to free the pulmonary areas from the shadows of the scapulae.

Pulmonary lesions, and in particular lesions of the glands round the hilum, are not uncommon as a sequel to trauma of the lungs when this has been caused by an unextracted bullet.

In some localities, such as Lorraine, where there is a dense industrial population, pneumokonioses are very common in the form of anthracosis, chalicosis and siderosis. These lesions may persist for years in patients after leaving the unhealthy occupations which caused the disease. The author especially shows positive proofs of a case of chalicosis complicated by pulmonary tuberculosis in a stonemason who had left his trade five years previously. One might have thought that a mass of large flints with rounded and sharp edges was formed at the level of the hilum of the lungs and of the entrance of the large bronchi. P. L.-B.

## *Radiotherapy*

**Schaeffer, F.**, and **Chotzen, T.** **Radiotherapy of tumours of the hypophysis and of acromegaly.** *Strahlentherapie,* 1920, Jan. 1, p. 190. (*J. de radiol. et d'électrol.*, 1921, **5**, 41.)

The authors have treated eight cases of tumour of the hypophysis and of acromegaly, and publish detailed observations with photographs and statements of the visual field, showing the results of treatment in the seven cases submitted to radiotherapy. In one a real clinical recovery for two years can be spoken of, and in three others there has been great benefit; lastly, in the case of one patient, arrest of the process in evolution which has remained stationary for more than a year was noted, and in another case, in which the diagnosis in other respects was very doubtful, radiotherapy did not seem to have any effect.

One case alone, a very advanced case, was not treated by radiotherapy but by radium therapy, the application having been made with 50 mgm. of radium bromide placed for 12 and then 48 hours in the sphenoidal sinus previously opened surgically.

These applications have been repeated seven times, from June 1915 to January 1918, without any other result than the appearance of a perforation of the soft palate about the size of a shilling.

As regards technique, the authors have only used as a rule, as paths of entry, the frontal and temporal regions over a depth of four to five centimetres, dividing them on each side into four rectangles or eight ports of entry in all, the distance of the anticathode from the skin being 30 centimetres. The total irradiation was distributed over three to five days and repeated at first every fortnight and later every four, six, or eight weeks.

Filtration: at first 3 mm. of aluminium, later 0·5 mm. of zinc. Dose: at first two Sabouraud-Noirés, later measured with the meter of Fürstenau. There is need to mention that young patients appear to afford much better and more rapid results than old patients. P.-L.-B.

**Japiot, P.**, et **Bussy, L.** Une technique simplifiée de la radiothérapie oculaire. [**A simplified technique for radiotherapy of the eye.**] *Arch. d'électric. méd.*, 1921, **29**, 65.

The authors here deal with treatment of affections of the eye itself rather than with ocular tumours. A precise technique has yet to be found, but they have treated cases successfully. The harmful action of the rays on the eyelashes and on the eye itself necessitate the use of small doses, especially in the case of children, whose eyes are much more sensitive than those of adults. The method of limiting the irradiation to the cornea by means of an apparatus consisting of a pierced lead protector and a blepharostat frighten the child and the cornea is constantly moving out of the field of irradiation. The authors therefore used penetrating rays in weak doses. The child is extended on his back with his head immobilized. The rays are directed on the whole of the affected eye. If both eyes be affected the face is irradiated in a transverse band across the eyes and the bridge of the nose. The latter can if necessary be protected by a soft lead plate covered, on the side touching the skin, by gauze or celluloid to stop the secondary rays. As filter, they used almost exclusively 3 mm. aluminium. The child can thus be at his ease and can close his eyes without hindering the irradiation. Research is still necessary on the question of dose. The authors used, with success, very weak repeated doses, generally five irradiations at intervals of a week, each about a quarter of an hour under filter. They consider a precise dose to be unnecessary, since the doses are so small as to make hardly appreciable differences in the results obtained. The hardness of the rays and the duration of the séances are the most important factors. S. U. L.-B.

## *Radium Therapy*

**Schmidt, V.** Sarkom opstaaet ved Radiumbehandling af Epitheliom paa Tungen. [**Sarcoma following radium treatment of epithelioma of the tongue.**] *Hosp.-Tid.*, 1921, **64**, 53.

Schmidt's case was that of a woman, aged 56, from the margin of whose tongue an epithelioma was removed in 1916. In 1918 a relapse occurred, for which she was repeatedly treated with radium. The tumour disappeared completely from the margin of the tongue, but as a direct sequel to this treatment an inflammatory reaction developed in the alveolar-lingual sulcus, extending to the cicatrix in the tongue. The infiltration spread outwards to the alveolar process, and a soft tumour, of the size of the kernel of a nut, budded out from this infiltration. On excision and microscopy, it proved to be a sarcoma. C. L.

**Shaw, W. F.** and **Burrows, A. Wertheim's hysterectomy for advanced carcinoma of the cervix made possible by the use of radium.** *Proc. Roy. Soc. Med.*, 1920, **13** (Section of Obstetrics and Gynaecology), 191–8.

The greatest advance made in the treatment of carcinoma of the cervix since the general adoption of Wertheim's radical operation has been the introduction of the therapeutic use of radium, by which the operability of the disease is definitely increased. Operation was undertaken at periods varying from two to three months after the application of radium. One sitting was usually enough, but occasionally two were given. The technical difficulty of the operation is materially increased, the growth being replaced by hard cartilaginous material, and in cases where this had extended completely round the ureters or on to the bladder completion of the operation was impossible.

In using the radium many tubes must be buried in the cervix and surrounding tissues and the largest possible dose must be used. No uniformity of good results can be obtained by using less than 120 mgm. of radium element or millicuries of emanation. At least 20 per cent. of inoperable cases of carcinoma of the cervix come within the range of surgery after radium treatment.

Details of eight cases are given. E. M. W.

**Roy, M. P. L. J.** De la curiethérapie dans le traitement du cancer du col utérin. [**Radium treatment of cancer of the cervix uteri.**] *Thèse*, Nancy, 1920. (*J. de radiol. et d'électrol.*, 1921, **5**, 140.)

With the aid of ten observations, the author demonstrates the efficacy of radium in the treatment of certain cases of cancer of the cervix uteri. Radium, used in convenient doses, effects in the cancerous tissues a cytolysis followed by resorption by the lymphatic system. These tissues seem all the more sensitive to this action as their cells are less differentiated. From this point of view cancer of the neck of the uterus may be classified in the following order of radium sensibility: (1) squamous epitheliomata, metatypical and atypical; (2) cylindrical epitheliomata; (3) typical squamous epitheliomata.

On the other hand, there seems to exist a particular sensibility of the neoplasms, which depends on their shape, the ordering of their tissue and of their stroma; it also appears that this sensibility varies with each subject, with her constitution and general health. The forms of neoplasm, classified in order of sensibility, are as follows: (1) vegetant; (2) ulcerous; (3) primitive endocavital; (4) liminary; (5) scirrhous.

In the present state of our knowledge, radium therapy should only be used in association with surgery, and this combination should comprise:

(1) A preliminary treatment by radium to prepare the way for operation and to lessen the chances of implantation and of blood metastasis.

(2) Surgical intervention to eliminate all that is microscopically visible of the tumour.

(3) A second application of radium to kill the epitheliomatous cells inevitably left by the operation and not sufficiently affected by the former application of radium. With radium surgery, the best results are obtained in early-diagnosed cases of cancer of the neck of the uterus. For purposes of treatment these neoplasms may be divided as follows:

(1) Cancer strictly limited to the neck. The author considers that the results obtained from radium therapy, already good, will be regarded 'with enthusiasm' when time shall have proved them to be real cures. According to certain surgeons (Hartmann), these cases may perhaps accrue only when radium has been employed.

(2) Cases surgically at or about the limit of operation. An application of radium can change them into operable cases in which cure may be hoped for; or perhaps radium is the only treatment possible, though, in spite of happy exceptions, it can only effect a temporary regression.

(3) Extreme cases for which radium is often contra-indicated since it may cause fistulae, stimulate metastasis, or determine dangerous and even fatal toxic resorptions.

(4) Relapse. Application of radium may be made, at a sufficiently prolonged interval after operation in cases of post-operative relapse, but it will have much less influence on post-radiation relapse.

The greatest success with radium is in cases limited to the neck of the uterus, whether as an aid to surgery, or alone; but only the future can show whether the method of isolated radium therapy is without danger and should become general, and if the technique, which is not yet definitely stabilized, can by itself conquer the evolution of cancerous growths.

S. U. L.-B.

## *Radiobiology.*

**Bagg, H. J., Ewing, J.,** and **Quick, D. An experimental study of the effects of radium emanation on the brains of animals.** *J. Nerv. & Ment. Dis.*, 1921, **53**, 127.

The experiments described below were communicated to the New York Neurological Society on December 7, 1920. The investigation was undertaken in order to determine a suitable technique for the use of radium emanation as a therapeutic agent in cases of brain tumour. Three points had to be investigated: (1) The nervous tissue reaction from a histological point of view of the normal brain; (2) dosage, to find the amount of emanation the normal brain could stand without damage; (3) the most practical method of applying the emanation. Four methods were (*a*) unfiltered emanation in minute quantities—0·2 to 1·5 millicuries permanently inserted beneath the scalp in rats and directly inserted into the brain in other small animals; (*b*) unfiltered emanation, 63 to 255 millicuries inserted into the brain of rabbits and dogs for various lengths of time; (*c*) a comparatively large amount of emanation filtered by 1 mm. of lead placed in the brain of a dog for 35 mins.; (*d*) doses of emanation corresponding to 4,000 and 9,000 millicurie hours applied externally over the heads of two dogs and 12,030 millicurie hours over the left temporal region in a monkey, in all cases heavily filtered. A short account of the technique is given.

The most interesting results were: (1) a very localized effect of radium destruction when small doses of unfiltered emanation were embedded in the brain, accompanied by a marked polynuclear infiltration round the necrotic area. (2) A much greater amount of destruction with large doses of unfiltered emanation embedded for a short time than with small doses for a long time although the number of millicurie hours was the same; (3) comparatively slight damage after the application of large heavily filtered doses applied externally. In method (*a*) a considerable area of brain tissue was destroyed without any discerned neurological disturbances, but the same number of millicurie hours applied as a comparatively large dose for a short time produced pronounced neurological disturbances, generally fatal in a few days. The results of method (*d*) showed that the normal brain is markedly resistant to exposure to the $\gamma$-rays of radium emanation.

Of the four methods investigated, the surface application of heavily filtered emanation and the embedding of small doses of unfiltered emanation are considered the best.

Ewing discussed the types of tumour that have been treated by radiation. He stated that neuro-fibromata and neuro-sarcomata belonged to the class of tumours resistant to radiation; if surgical methods are not successful in their removal, little help from physical agents can be expected. Psammomata, since usually subdural, might be affected by radium, especially if it be applied directly to the tumour: true angioendotheliomata or peritheliomata should be more susceptible to radium. Angiosarcomata should be markedly affected by radiation since their nutrition is unstable. Gliomata present most of the structural features that favour susceptibility to radiation. Primary carcinoma of the brain from its structure should have a high susceptibility to radium.

Quick's paper dealt with the clinical results of treatment of nerve tissue tumours by radium. He stated that most of the cases treated by radium had been pituitary tumours, and it was agreed that the pressure symptoms can be greatly relieved unless due to cysts. A short account of his results on various types of tumours is given. He states that surgery and radium should be combined, but that an operation should not be performed unless radium can be applied at the same time and if possible buried in the tumour.

In the discussion that followed Frazier pointed out a number of points in which malignant tumours of the brain differed from those in other parts. He spoke of three cases which had been under observation for seven, six, and four years respectively. Radium therapy in pituitary lesions was discussed and it was pointed out that after sellar decompression radium could be applied close to the lesion: he believed that in these lesions a simple subsellar decompression followed by X-ray treatment was the best. His conclusions were that the best results had been obtained in pituitary lesions and endotheliomata, that there was no evidence to show that radium had any effect on gliomata: that radium is now employed as a prophylactic against recurrence after removal of the growth; as a prophylactic against recurring visual disturbances after sellar decompression; as an active agent by direct implantation in all inoperable growths exposed on the table; as an inactive agent by indirect application in all inoperable growths.

Pancoast gave an account of experiments on the brains of normal dogs; $\gamma$-rays alone were used in doses varying from 300–900 milligramme hours. The results showed that comparatively large doses could be employed without serious destruction of brain tissue surrounding a tumour. Other experiments were carried out by Prendergass in which two dogs were subjected to the implantation of radium into the motor cortex; 2,100 milligramme hours and 2,500 milligramme hours respectively was the dose. Both dogs died in about a month; there was no paralysis. The adjacent brain was congested and indurated. The application of a safe technique demanded the following: (1) a knowledge of the type of growth; (2) a knowledge of the relative amount of radiation required; (3) the size of the growth from centre to periphery if central implantation is to be practised; (4) if the growth is irregular the normal brain must be carefully guarded; (5) it is best to give an under dose by implantation supplemented by cross-firing from outside the head; (6) Frazier and Pancoast do not advocate the implantation of needles at the actively growing periphery with the present state of knowledge of their effects. For treatment tumours may be grouped into: (1) Inoperable tumours found at operation. (2) Tumours found at operation and partly removed. (3) Tumours not localized or found at operation, or inaccessible at operation. (4) Pituitary growths. For (1) and (2) central implantation supplemented by cross-fire from outside is advocated; for (3) cross-fire in all possible directions; for (4) radium treatment after sellar decompression, supplemented by cross-fire through each temporal region.

Abbe said he had only had three cases under treatment, all post-operative cases of gliosarcoma; he thought no benefit had occurred after radium treatment. He thought the best treatment would be to apply 20–50 milligrammes of radium in a sterile tube without filtration directly to the tumour for 30 minutes and then close the wound. In fibrosarcoma of the dura mater he had found no benefit from the use of radium: he had never seen cerebral disturbances after the external application of radium in human subjects. He had treated four cases of syringomyelia, three without benefit and one with very beneficial results.

Strauss said that the direct radiation of tumours at the surface of the brain and where their removal would incapacitate the patient were advantageous. In pituitary lesions radium applied in the nasopharynx should follow sellar decompression; enough radium should be used to go through the sphenoid. Ewing thinks that if used early enough radium is sufficiently penetrating to use without decompression. Since surgery does not cure cases of glioma, radiotherapy should be tried, and, when more knowledge on the subject has been obtained, may be a means of treating these growths successfully.

Abrahamson said it was important to discover what effect radium produced on the choroid plexus and cerebrospinal fluid. P. L.-B.

## *Electro-technique.*

**D'Halluin, M.** L'électricité qui tue. Comment on meurt. Comment on peut sauver. [**Electric currents which kill. The mode of death. How life may be saved.**] *J. de radiol. et d'électrol.*, 1920, **4**, 254.

The measures to be taken in dealing with cases of apparent death by electricity depends upon the nature of the effects produced by the current. These are primarily of two classes, respiratory and cardiac, the former being the better known. The latter case is often ignored, although there can be no doubt of its existence, and its serious character is due to the persistence of fibrillation.

Fibrillation is to be distinguished from another form of myocardiac disturbance, denominated 'folie ondulatoire' by the author, in which there is a wave-like contraction of the whole organ. The importance of the distinction lies in the fact that a heart showing the 'folie ondulatoire' may recover a normal rhythm under normal physiological conditions, whereas a fibrillating heart is incapable of such recovery. Hence the grave importance of fibrillation. This rule holds for all the larger animals, including man; the only exceptions from it are found in small animals such as rats, guinea-pigs, and rabbits.

The ready response of the heart to weak currents explains why under certain conditions low tension currents may lead to certain death. High tension currents on the other hand inhibit the medulla and do not affect the heart directly. Death by electricity is usually attributed to inhibition. In the dog low tension currents, up to about 120 volts, arrest the heart by fibrillation while respiration continues for some moments longer. Currents of 240–600 volts produce the two effects simultaneously, and high tension currents of 1,200–4,800 volts kill by inhibition of the medulla pure and simple—in fact, cause death by asphyxia. Hence it is to be seen that, given a good contact allowing the passage of a sufficient intensity of current, low tension currents, commonly considered comparatively harmless, are in fact the most dangerous. On the other hand, given a poor contact, the current transmitted from a low tension source is practically nil, while with a medium tension current enough may be transmitted to kill the heart though not to paralyse the medulla, but high tension currents will still transmit enough to inhibit respiration.

The ordinary accepted methods of treatment are often quite efficacious in dealing with purely respiratory disturbances, but cardiac disturbances, whether primary or secondary, can and should be diagnosed with precision, and require the prompt institution of cardiac massage. The question as to whether or not a heart is still beating is not always an easy matter to decide by ordinary clinical methods, but can readily be determined by the instillation of a drop of ether into the eye. The reaction occurring if the heart be still beating is a slight flush of the conjunctiva. It is essential for the purposes of this test that the patient be placed in a horizontal position and that artificial respiration be discontinued since the circulation resulting from the rhythmic compression of the thorax is sufficient to vitiate the test. The instillation of dionin has a similar effect. The diagnosis of ventricular fibrillation can be made when, immediately after the accident, venous pulsation in the neck is observed in association with apparent absence of all ventricular movement. The absence of the venous pulse is of no diagnostic value since it may happen that the auricles are also fibrillating.

Direct cardiac massage is the only effective way of dealing with a heart which has stopped beating, and the blood in the circulation so produced must be kept well oxygenated. Massage of the heart may initiate fibrillation in an asphyxiated heart, and is certain to do so if fibrillation was the cause of cardiac arrest.

Intravenous injections of potassium chloride provide a ready and simple means of combating fibrillation. These injections are to be made into the jugular vein and must invariably be used in conjunction with cardiac massage. A 5 per cent. solution is used and the quantity injected must be sufficient (1) to produce an initial paralysis of the cardiac muscle fibres, and (2) to maintain a sedative effect upon the muscle after the injected solution has become diffused throughout the circulation. After such an injection cardiac massage must be continued for five or ten minutes, or even longer, and rhythmic muscular contractions of the myocardium will then reappear. The toxicity of potassium chloride is a function of the rate of injection rather than of the total amount of salt injected. Thus in dogs the lethal dose is 14 cgm. per kilogramme of body-weight if injected at the rate of 20 mgm. per kilogramme per minute, but is 42 cgm. per kilogramme when injected at the rate of 4 mgm. per kilogramme per minute.

The results of experiments on dogs gave a revival rate of 37 per cent. when cardiac massage alone was used and instituted five minutes after arrest of the heart, and a rate of 65 per cent. when injections of potassium chloride were used in conjunction with the massage, although massage was not begun until 10 or 15 minutes after arrest of the heart.

E. M. W.

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